```
=> fil reg
FILE 'REGISTRY' ENTERED AT 07:56:53 ON 21 DEC 2005
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   19 DEC 2005  HIGHEST RN 870234-75-6
DICTIONARY FILE UPDATES:  19 DEC 2005  HIGHEST RN 870234-75-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

**********************************************************************
*                                                                    *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                    *
**********************************************************************

Structure search iteration limits have been increased.  See HELP SLIMITS
for details.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> d 133 ide can tot

L33  ANSWER 1 OF 2  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   51481-61-9  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   Guanidine, N-cyano-N'-methyl-N''-[2-[[(5-methyl-1H-imidazol-4-
     yl)methyl]thio]ethyl]- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Acibilin
CN   Acinil
CN   Biomet
CN   Cimal
CN   Cimetag
CN   Cimetidine
CN   Cimetum
CN   Dyspamet
CN   Edalene
CN   Eureceptor
CN   Gastromet
CN   Histodil
CN   N-Cyano-N'-methyl-N''-[2-((4-methyl-5-imidazolyl)-
     methylthio)ethyl]guanidine
```
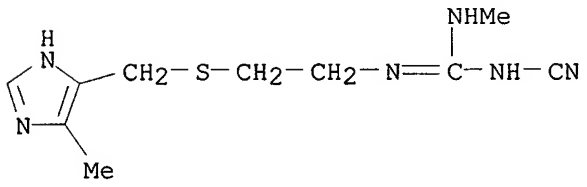

CN NSC 335308
CN Peptol
CN SKF 92334
CN Tagamet
CN Tametin
CN Tratul
CN Ulcedin
CN Ulcedine
CN Ulcerfen
CN Ulcimet
CN Ulcofalk
CN Ulcomedina
CN Ulcomet
CN Ulhys
FS 3D CONCORD
MF C10 H16 N6 S
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4975 REFERENCES IN FILE CA (1907 TO DATE)
74 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4979 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 143:483154

REFERENCE 2: 143:475514

REFERENCE 3: 143:474444

REFERENCE 4: 143:466252

REFERENCE 5: 143:466186

REFERENCE 6: 143:458512

REFERENCE 7: 143:453279

REFERENCE 8: 143:452893

REFERENCE 9: 143:452734

REFERENCE 10: 143:452184

L33 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2005 ACS on STN
RN **50-63-5** REGISTRY
ED Entered STN: 16 Nov 1984
CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl-, phosphate (1:2) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Quinoline, 7-chloro-4-[(4-diethylamino-1-methylbutyl)amino]-, diphosphate (6CI)
CN Quinoline, 7-chloro-4-[[4-(diethylamino)-1-methylbutyl]amino]-, phosphate (1:2) (8CI)
OTHER NAMES:
CN (±)-Chloroquine diphosphate
CN 3377RP
CN 7-Chloro-4-[(4'-diethylamino-1-methylbutyl)amino]quinoline diphosphate
CN Aralen diphosphate
CN Aralen phosphate
CN Arechin
CN Avloclor
CN Bemaphate
CN Chingamin
CN Chingamin phosphate
CN Chlorochin diphosphate
CN Chloroquin diphosphate
CN Chloroquine dihydrogen phosphate (1:2)
CN Chloroquine diphosphate
CN **Chloroquine phosphate**
CN Delagil
CN dl-Chloroquine diphosphate
CN Gontochin phosphate
CN Imagon
CN Khingamin
CN Malaquin
CN Nivaquine B
CN NSC 14050
CN Quingamine
CN Resochin
CN Resoquine
CN Sanoquin
CN SN 7618
CN Tanakan
CN Tanakan (antimalarial)
CN Tresochin
CN WR 1522
DR 69698-56-2, 6384-82-3
MF **C18 H26 Cl N3 . 2 H3 O4 P**
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DIOGENES, EMBASE, HODOC*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, NIOSHTIC, PROMT, PS, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

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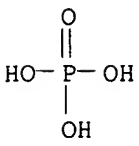
CMF H3 O4 P



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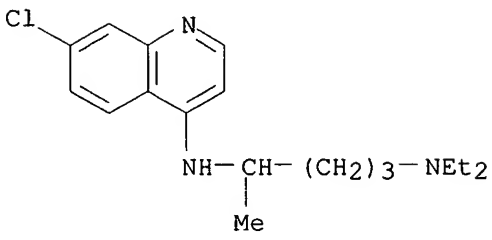

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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4 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
759 REFERENCES IN FILE CAPLUS (1907 TO DATE)
19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 143:452940

REFERENCE 2: 143:446301

REFERENCE 3: 143:432094

REFERENCE 4: 143:427563

REFERENCE 5: 143:422486

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REFERENCE 9: 143:179241

REFERENCE 10: 143:159583

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L2          1574 S E3-E52
               E NELSON JODI/AU
L3            16 S E3-E5
               E ALPHA/PA,CS
               E ALPHA RES/PA,CS
L4             1 S E13-E16
L5             3 S L1,L4

     FILE 'REGISTRY' ENTERED AT 07:45:14 ON 21 DEC 2005
               E CHLOROQUINE PHOSPHATE/CN
L6             1 S E3
L7            24 S 54-05-7/CRN AND P/ELS
L8            20 S L7 AND 7664-38-2/CRN
L9             4 S L7 NOT L8
               E CIMETIDINE/CN
L10            1 S E3
L11           69 S 51481-61-9/CRN
L12            0 S L11 AND L8
L13            6 S L8 NOT MXS/CI
L14           41 S L11 NOT MXS/CI
L15           11 S L14 NOT (COMPD OR CONJUGATE OR WITH)
L16           30 S L14 NOT L15
L17            6 S L6,L13
L18           12 S L10,L15

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L20          667 S (CHLOROQUIN# OR CHLORCHIN#)()(PHOSPHATE OR DIPHOSPHATE OR DIH
L21          234 S AVLOCLOR OR ARECHIN OR ARALEN()(PHOSPHATE OR DIPHOSPHATE) OR
L22           14 S SN 7618 OR NSC 14050 OR WR 1522 OR SN7618 OR NSC14050 OR NSC
L23         1069 S L19-L22
L24         5067 S L18
L25         8050 S CIMETIDIN# OR ACIBILIN OR ACINIL OR BIOMET OR CIMAL OR CIMETA
L26            0 S SKF92334 OR SKF 92334 OR SKF 92 334 OR NSC335308 OR NSC 33530
L27         8253 S L24-L26
L28            9 S L23 AND L27
L29            3 S L28 AND L1-L5
L30            7 S L28 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L31            4 S L30 NOT L29
               SEL HIT RN L29

     FILE 'REGISTRY' ENTERED AT 07:56:34 ON 21 DEC 2005
L32            2 S E1-E2
L33            2 S L32 AND L17,L18

     FILE 'REGISTRY' ENTERED AT 07:56:53 ON 21 DEC 2005

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 07:57:00 ON 21 DEC 2005
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FILE COVERS 1907 - 21 Dec 2005 VOL 143 ISS 26
FILE LAST UPDATED: 20 Dec 2005 (20051220/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for substance identification.

=> d l29 bib abs hitstr retable tot

11 species

L29 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 20(
AN 2004:995776 HCAPLUS
DN 141:406120
TI Compositions and methods for the trea tardive dyskinesias with quinoline ri compounds
IN **Nelson, Jodi**
PA USA
SO U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S. Ser. No. 192,414.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004229908	A1	20041118	US 2003-616692	20030709 <--
	US 6417177	B1	20020709	US 2000-615639	20000713
	US 2002198231	A1	20021226	US 2002-192414	20020709
PRAI	US 1999-143767P	P	19990713		
	US 2000-175051P	P	20000107		
	US 2000-202140P	P	20000505		
	US 2000-615639	A2	20000713		
	US 2002-192414	A2	20020709		
	US 2003-479748P	P	20030619		

AB This invention provides compns. and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration, as well as drug-induced dyskinesias, tardive dyskinesia, Neuroleptic Malignant Syndrome, and neg. symptoms of schizophrenia. An effective amount of a neuromelanin-binding composition having a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-**chloroquine diphosphate**. Selected adjuvants are also provided as part of the compns. of this invention.

IT **50-63-5, Chloroquine diphosphate**
51481-61-9, Cimetidine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

RN 50-63-5 HCAPLUS
CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl-, phosphate (1:2) (9CI) (CA INDEX NAME)

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CRN 7664-38-2
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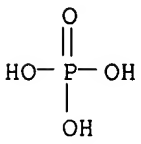

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CRN 54-05-7
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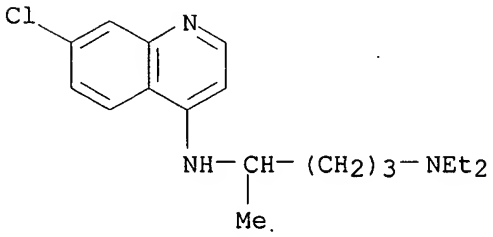
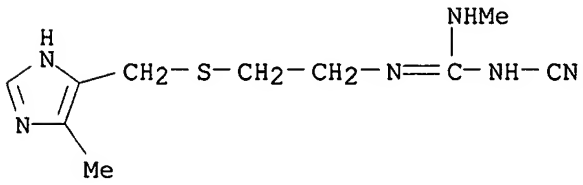


RN 51481-61-9 HCAPLUS
CN Guanidine, N-cyano-N'-methyl-N''-[2-[[(5-methyl-1H-imidazol-4-yl)methyl]thio]ethyl]- (9CI) (CA INDEX NAME)



L29 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:41228 HCAPLUS
DN 140:105304
TI Compositions and methods for the treatment of Parkinson's disease and tardive dyskinesias
IN **Nelson, Jodi**
PA **Alpha Research Group, L.L.C., USA**

SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004004660	A2	20040115	WO 2003-US21463	20030709
	WO 2004004660	A3	20051103		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2002198231	A1	20021226	US 2002-192414	20020709
	EP 1581167	A2	20051005	EP 2003-763398	20030709
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-192414	A	20020709		
	US 2003-479748P	P	20030619		
	US 1999-143767P	P	19990713		
	US 2000-175051P	P	20000107		
	US 2000-202140P	P	20000505		
	US 2000-615639	A2	20000713		
	WO 2003-US21463	W	20030709		

AB This invention provides compns. and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration, as well as drug-induced dyskinesias, tardive dyskinesia, Neuroleptic Malignant Syndrome, and neg. symptoms of schizophrenia. An effective amount of a neuromelanin-binding composition having a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-**chloroquine diphosphate.** Selected adjuvants are also provided as part of the compns. of this invention.

IT **50-63-5, Chloroquine phosphate**
51481-61-9, Cimetidine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for treatment of Parkinson's disease and tardive dyskinesias)

RN 50-63-5 HCAPLUS
CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl-, phosphate (1:2) (9CI) (CA INDEX NAME)

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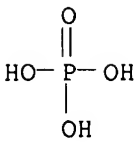
CRN 7664-38-2
CMF H3 O4 P



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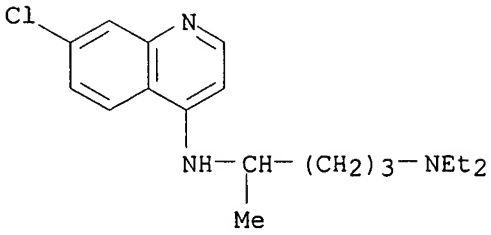
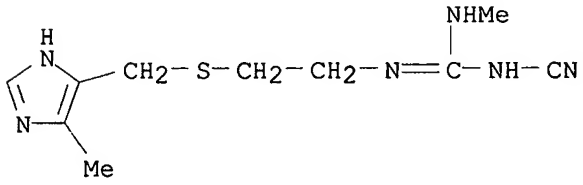


RN 51481-61-9 HCAPLUS
CN Guanidine, N-cyano-N'-methyl-N''-[2-[[(5-methyl-1H-imidazol-4-yl)methyl]thio]ethyl]- (9CI) (CA INDEX NAME)



L29 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:978470 HCAPLUS
DN 138:33365
TI Compositions and methods for the treatment of Parkinson's disease with quinoline ring-containing neuromelanin-binding compounds
IN **Nelson, Jodi**
PA USA
SO U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. 6,417,177.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002198231	A1	20021226	US 2002-192414	20020709
	US 6417177	B1	20020709	US 2000-615639	20000713
	WO 2004004660	A2	20040115	WO 2003-US21463	20030709
	WO 2004004660	A3	20051103		

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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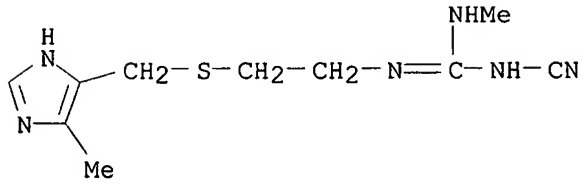
US 2000-175051P P 20000107
US 2000-202140P P 20000505
US 2000-615639 A2 20000713
US 2002-192414 A 20020709
US 2003-479748P P 20030619
WO 2003-US21463 W 20030709

AB This invention provides compns. and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration. An effective amount of a neuromelanin-binding composition having a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-chloroquine. Selected adjuvants are also provided as part of the compns. of this invention.

IT **51481-61-9, Cimetidine**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytochrome P 450 2D6 and A3 inhibitor inhibiting peripheral metabolism of chloroquine compds.; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

RN 51481-61-9 HCAPLUS

CN Guanidine, N-cyano-N'-methyl-N''-[2-[[(5-methyl-1H-imidazol-4-yl)methyl]thio]ethyl]- (9CI) (CA INDEX NAME)



IT **50-63-5, Chloroquine phosphate**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

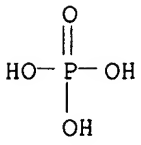
RN 50-63-5 HCAPLUS

CN 1,4-Pentanediamine, N4-(7-chloro-4-quinolinyl)-N1,N1-diethyl-, phosphate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 7664-38-2

CMF H3 O4 P



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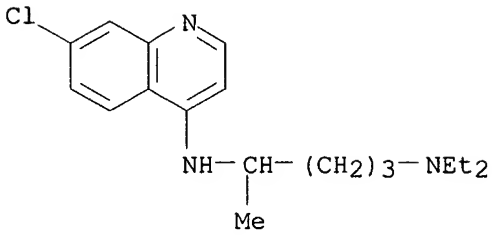

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E NELSON JODI/AU
L3 16 S E3-E5
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E ALPHA RES/PA,CS
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L5 3 S L1,L4

FILE 'REGISTRY' ENTERED AT 07:45:14 ON 21 DEC 2005
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L6 1 S E3
L7 24 S 54-05-7/CRN AND P/ELS
L8 20 S L7 AND 7664-38-2/CRN
L9 4 S L7 NOT L8
E CIMETIDINE/CN
L10 1 S E3
L11 69 S 51481-61-9/CRN
L12 0 S L11 AND L8
L13 6 S L8 NOT MXS/CI
L14 41 S L11 NOT MXS/CI
L15 11 S L14 NOT (COMPD OR CONJUGATE OR WITH)
L16 30 S L14 NOT L15
L17 6 S L6,L13

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L18          12 S L10,L15

     FILE 'HCAPLUS' ENTERED AT 07:49:45 ON 21 DEC 2005
L19          771 S L17
L20          667 S (CHLOROQUIN# OR CHLORCHIN#)()(PHOSPHATE OR DIPHOSPHATE OR DIH
L21          234 S AVLOCLOR OR ARECHIN OR ARALEN()(PHOSPHATE OR DIPHOSPHATE) OR
L22           14 S SN 7618 OR NSC 14050 OR WR 1522 OR SN7618 OR NSC14050 OR NSC
L23         1069 S L19-L22
L24         5067 S L18
L25         8050 S CIMETIDIN# OR ACIBILIN OR ACINIL OR BIOMET OR CIMAL OR CIMETA
L26            0 S SKF92334 OR SKF 92334 OR SKF 92 334 OR NSC335308 OR NSC 33530
L27         8253 S L24-L26
L28            9 S L23 AND L27
L29            3 S L28 AND L1-L5
L30            7 S L28 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L31            4 S L30 NOT L29
                 SEL HIT RN L29

     FILE 'REGISTRY' ENTERED AT 07:56:34 ON 21 DEC 2005
L32            2 S E1-E2
L33            2 S L32 AND L17,L18

     FILE 'REGISTRY' ENTERED AT 07:56:53 ON 21 DEC 2005

     FILE 'HCAPLUS' ENTERED AT 07:57:00 ON 21 DEC 2005

     FILE 'REGISTRY' ENTERED AT 07:57:25 ON 21 DEC 2005
                 E 591.79/RID
                 E 591.79.52/RID
L34        363017 S E3
L35             6 S (CELECOXIB OR CHLORPHENIRAMINE OR FLUOXETINE OR PAROXETINE OR
L36             9 S (AMIODARONE OR CLOMIPRAMINE OR LEVOMEPROMAZINE OR METOCLOPRAM
L37             9 S (INDINAVIR OR NELFINAVIR OR SAQUINAVIR OR AMIODARONE OR CIPRO
L38             6 S (FLUVOXAMINE OR ITRACONAZOLE OR KETOCONAZOLE OR MIFEPRISTONE
                 E DELAVIRIDINE/CN
L39             1 S E1
                 E NORFLOXACINEM/CN
L40             1 S E2
                 E DIETHYL DITHIOCARBAMATE/CN
                 E DITHIOCARBAMATE/CN
                 E C5H11NS2/MF
L41            69 S E3
L42             4 S L41 AND DIETHYL
L43             2 S L42 NOT (13C OR LABELED)
L44            33 S L35-L40,L43

     FILE 'HCAPLUS' ENTERED AT 08:07:30 ON 21 DEC 2005
L45              TRA L29 1- RN :      233 TERMS

     FILE 'REGISTRY' ENTERED AT 08:07:31 ON 21 DEC 2005
L46          233 SEA L45
L47           32 S L46 AND L44
L48            1 S L44 NOT L47
                 SEL RN L47
L49         1862 S E1-E32/CRN
L50         1189 S L49 NOT (MXS OR PMS OR IDS)/CI
L51          364 S L50 NOT (COMPD OR WITH OR LABELED OR CONJUGATE)
L52          354 S L51 NOT H
L53           10 S L51 NOT L52
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L54       10279 S L52
L55       61759 S L47
L56       14065 S CELECOXIB OR CHLORPHENIRAMIN# OR  FLUOXETINE OR PAROXETINE OR
L57       19948 S AMIODARONE OR CLOMIPRAMINE OR LEVOMEPROMAZINE OR METOCLOPRAMI
L58       42458 S INDINAVIR OR NELFINAVIR OR SAQUINAVIR OR AMIODARONE OR CIPROF
L59        8909 S FLUVOXAMINE OR ITRACONAZOLE OR KETOCONAZOLE OR MIFEPRISTONE O
L60        1019 S DELAVIRDINE OR NORFLOXACINEM OR DIETHYL DITHIOCARBAMATE
L61       10445 S DIETHYLDITHIOCARBAMIC ACID OR DIETHYLDITHIOCARBAMATE
L62      101369 S L27,L54-L61

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L63         142 S L34 AND L46 NOT L47,L52
L64         141 S L63 NOT L17

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L65        5629 S L64
L66        6449 S L23,L65

     FILE 'REGISTRY' ENTERED AT 08:14:19 ON 21 DEC 2005
L67      362658 S L34 NOT L6,L7,L44,L47,L49
L68      312879 S L67 AND 1/NC
L69      306617 S L68 NOT (PMS OR CCS OR IDS OR MNS)/CI
L70      306104 S L69 NOT SQL/FA
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L72      201038 S L70 NOT L71
L73        9075 S L72 AND ED<=2000

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L74       83387 S L71
L75        1650 S L73
L76       13929 S (A61K031-47 OR C07D215)/IPC
L77       93905 S L66,L74-L76
L78        4834 S L77 AND L62
L79        3464 S L78 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L80           4 S L78 AND L1-L5

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L81           2 S 329322-82-9 OR 330597-62-1

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L82          45 S L81 AND L77
L83           3 S L82 AND L1-L5
L84           4 S L80,L83
L85           7 S L82 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L86        3463 S L79,L85 NOT L84
                E NERVOUS SYSTEM/CT
L87      333287 S E3+OLD,NT
L88           8 S E2
L89      103409 S E3-E96
L90       33636 S E99-E204
L91        9577 S E96,E97,E205-E216
L92      224670 S E240+OLD,NT
L93       13731 S E240-E300
L94        3347 S E301-E318
L95        1367 S E319-E329
                E NEURON/CT
L96       19335 S E3
L97           1 S E57
                E SCHIZOPHRENIA/CT
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L98        10378 S E3-E7 OR E3+OLD,NT
                 E PARKINSON/CT
L99        15152 S E7-E9 OR E7+OLD,NT
                 E E7+ALL
                 E E13+ALL
L100        4895 S E4
                 E E12+ALL
                 E E14+ALL
L101        1219 S E5+NT
                 E E4+ALL
L102       22498 S E4+NT
                 E NERVE/CT
L103      167288 S E3+OLD,NT
L104      145870 S E3-E48
L105       34989 S E49-E96
L106       51767 S E97-E132
L107       30329 S E133-E180
L108       17918 S E181-E212
L109       11853 S E218-E228 OR E220+OLD,NT
L110       11092 S E229-E282
L111       52327 S E314 OR E317-E336 OR E319+OLD,NT
L112       14304 S E337-E372
L113       22876 S E373-E395
L114       13911 S E396
L115        1524 S E397-E401
                 E MOTOR/CT
L116         215 S E27
                 E COGNITI/CT
L117        9282 S E4+OLD,NT OR E4-E8 OR E11+OLD,NT OR E12
                 E E13+ALL
L118         996 S E2,E3
                 E MENTAL/CT
L119       14032 S E22,E23
L120       24566 S E29-E90
                 E E29+ALL
L121       58762 S E8+OLD,NT
                 E BRAIN/CT
                 E E3+ALL
L122      397625 S E4+OLD,NT
L123         218 S L86 AND L87-L122
L124           1 S L123 AND ?DYSKINES?
L125          12 S L123 AND ?PARKINSON?
L126           3 S L123 AND ?SCHIZOPHREN?
                 E METABOLISM/CT
                 E E13+ALL
L127          45 S E2,E3(L)PERIPHER?
L128         217 S E2+NT(L)PERIPHER?
L129           0 S L123 AND L127,L128
L130           2 S E2+OLD,NT AND L123
L131           4 S L84 AND L87-L122
L132           2 S L84 AND E2,E3
L133           4 S L131,L132
L134          15 S L124-L126
L135           1 S L134 AND L30
L136          14 S L134 NOT L135
                 SEL DN AN 7 9
L137           2 S L136 AND E1-E6

=> d all hitstr l137 tot
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L137 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1999:344848** HCAPLUS
DN **131:714**
ED Entered STN: 07 Jun 1999
TI Therapeutic uses of triazolo-pyridazine derivatives
IN Castro Pineiro, Jose Luis; Hefti, Franz Fridolin; Hill, Raymond George; McKernan, Ruth; Tattersall, Frederick David; Whiting, Paul John
PA Merck Sharp & Dohme Limited, UK
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-50
ICS A61K031-00; A61K045-06
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9925353	A1	19990527	WO 1998-GB3328	19981106 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9910415	A1	19990607	AU	[illegible] <--
	US 6174886	B1	20010116	US	
	US 6107296	A	20000822	US	
	US 6110915	A	20000829	US	
	US 6046196	A	20000404	US	
	US 6063783	A	20000516	US	
PRAI	GB 1997-23999	A	19971113	<--	
	GB 1997-26699	A	19971218	<--	
	GB 1997-26700	A	19971218	<--	
	GB 1997-26701	A	19971218	<--	
	GB 1997-26702	A	19971218	<--	
	GB 1998-1581	A	19980123	<--	
	WO 1998-GB3328	W	19981106	<--	

Broader context
[illegible] + 2nd component
+ date
+ use

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9925353	ICM	A61K031-50
	ICS	A61K031-00; A61K045-06
	IPCI	A61K0031-50 [ICM,6]; A61K0031-00 [ICS,6]; A61K0045-06 [ICS,6]
	ECLA	A61K031/5025 <--
AU 9910415	IPCI	A61K0031-50 [ICM,6]; A61K0031-00 [ICS,6]; A61K0045-06 [ICS,6] <--
US 6174886	IPCI	C07D0237-12 [ICM,7]; C07D0471-02 [ICS,7]; C07D0237-14 [ICS,7]
	NCL	514/248.000; 514/340.000; 544/236.000; 544/239.000
	ECLA	A61K031/5025 <--
US 6107296	IPCI	A01N0043-58 [ICM,7]; A01N0031-50 [ICS,7]
	NCL	514/248.000
	ECLA	A61K031/5025 <--
US 6110915	IPCI	A61K0031-495 [ICM,7]; A61K0031-50 [ICS,7]
	NCL	514/248.000

	ECLA	A61K031/5025 <--
US 6046196	IPCI	A61K0031-495 [ICM,7]; A61K0031-50 [ICS,7]
	NCL	514/248.000
	ECLA	A61K031/5025 <--
US 6063783	IPCI	A61K0031-495 [ICM,7]; A61K0031-50 [ICS,7]; A61K0031-54 [ICS,7]; A61K0031-415 [ICS,7]; A61K0031-34 [ICS,7]
	NCL	514/248.000; 514/226.500; 514/406.000; 514/473.000
	ECLA	A61K031/5025 <--

OS MARPAT 131:714

AB A class of substituted or 7,8-ring fused 1,2,4-triazolo[4,3-b]pyridazine derivs., possessing an optionally substituted cycloalkyl, Ph or heteroaryl substituent at the 3-position and a substituted alkoxy moiety at the 6-position, are selective ligands for GABAA receptors, in particular having high affinity for the α2 and/or α3 subunit thereof, and are accordingly of benefit in the treatment and/or prevention of psychotic disorders including **schizophrenia**; neurodegeneration arising from cerebral ischemia; pain; emesis; and muscle spasm or spasticity, e.g. in paraplegic patients.

ST triazolopyridazine deriv GABAA ligand therapeutic; antipsychotic **schizophrenia** analgesic antiemetic triazolopyridazine deriv; neurodegeneration cerebral ischemia triazolopyridazine deriv; muscle spasm spasticity triazolopyridazine deriv

IT 5-HT antagonists
(5-HT3; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT GABA agonists
(GABAA; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT GABA receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(GABAA; triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

IT Tachykinin receptors
(NK1 antagonists; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT Glutamate receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NMDA-binding, strychnine-insensitive glycine modulatory site of NMDA receptor; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT Opioids
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(analgesic; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT **Nerve**
(**degeneration**, from cerebral **ischemia**; triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

IT Neurotransmission
(glutamatergic, modulators; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT **Brain, disease**
(**ischemia**, neurodegeneration from; triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

IT Cytoprotective agents
(neuroprotectants; triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

IT Anti-inflammatory agents

(nonsteroidal; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT Drug delivery systems
(prodrugs; triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

IT Muscle relaxants
(spasmolytics; triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

IT Cholinergic antagonists
Dopamine antagonists
(triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT Analgesics
Antiemetics
Antipsychotics
Drug delivery systems
Muscle relaxants
(triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

IT 39391-18-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(2, inhibitors; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT 12794-10-4D, Benzodiazepine, derivs.
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GABAA receptor benzodiazepine binding site; triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

IT 56-40-6, Glycine, biological studies 57-24-9, Strychnine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(strychnine-insensitive glycine modulatory site of NMDA receptor; triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

IT 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies 52-86-8, Haloperidol 58-39-9, Perphenazine 69-23-8, Fluphenazine 113-59-7, Chlorprothixene 117-89-5, Trifluoperazine 1134-47-0, Baclofen 1977-10-2, Loxapine 2062-78-4, Pimozide 2751-68-0, Acetophenazine 3313-26-6, Thiothixene 5588-33-0, Mesoridazine 5786-21-0, Clozapine 7416-34-4, Molindone 15676-16-1, Sulpiride 71125-38-7, Meloxicam 106266-06-2, Risperidone 127625-29-0, Fananserin 131986-45-3, Xanomeline 132539-06-1, Olanzapine 146939-27-7, Ziprasidone 162011-90-7, Rofecoxib **169590-42-5**, **Celecoxib**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

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225642-16-0 225642-18-2 225642-21-7 225642-28-4
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triazolo-pyridazine derivative GABAA ligands, and therapeutic use)

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD

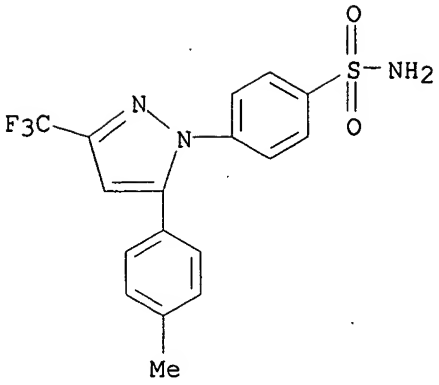
RE

(1) Anon; S-TRIAZOLO(3,4-a) (5, 6, 7, 8)TETRAHYDROPHTHA LAZINES 1978, 5, HCAPLUS
(2) Delini-Stula, A; JOURNAL OF PSYCHIATRIC RESEARCH 1996, V30(4), P239 MEDLINE
(3) Dunn, E; SOCIETY FOR NEUROSCIENCE ABSTRACTS 1995, V21(1-3), P2046
(4) Hadingham, K; MOLECULAR PHARMACOLOGY 1993, V43, P970 HCAPLUS
(5) Hall, E; JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM 1997, V17(8), P875 HCAPLUS
(6) Knoll Ag; WO 9632393 A 1996 HCAPLUS
(7) Lepetit Spa; EP 0085840 A 1983 HCAPLUS
(8) Merck Sharp & Dohme; WO 9834923 A 1998 HCAPLUS
(9) Mitsubishi Chemical Ind; JP 53021197 A 1978 HCAPLUS
(10) Richard, G; WO 9804559 A 1998 HCAPLUS
(11) Sanofi Sa; EP 0156734 A 1985 HCAPLUS
(12) Schering Ag; DE 19617862 A 1997 HCAPLUS
(13) Tarzia, G; FARMACO EDIZIONE SCIENTIFICA 1988, V43(2), P189 HCAPLUS

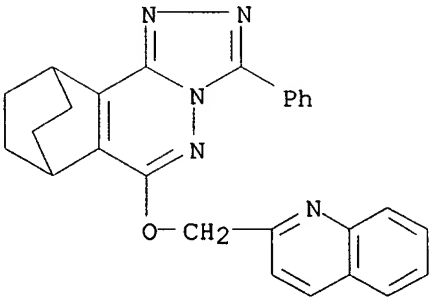
IT **169590-42-5, Celecoxib**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triazolo-pyridazine derivative GABAA ligands and therapeutic use, alone or with other compds.)

RN 169590-42-5 HCAPLUS

CN Benzenesulfonamide, 4-[5-(4-methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]- (9CI) (CA INDEX NAME)



IT **202929-64-4**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(triazolo-pyridazine derivative GABAA ligands, and therapeutic use)
RN 202929-64-4 HCAPLUS
CN 7,10-Ethano-1,2,4-triazolo[3,4-a]phthalazine, 7,8,9,10-tetrahydro-3-phenyl-6-(2-quinolinylmethoxy)- (9CI) (CA INDEX NAME)



L137 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1998:509091** HCAPLUS
DN **129:144869**
ED Entered STN: 17 Aug 1998
TI Serotoninergic 5-HT2B agonists for the treatment of depression and other CNS diseases
IN Kennett, Guy Anthony
PA Smithkline Beecham PLC, UK
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-00
CC 1-11 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9831354	A2	19980723	WO 1998-EP380	19980113 <--

W: CA, JP, US
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI GB 1997-899 A 19970117 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9831354	ICM	A61K031-00
	IPCI	A61K0031-00 [ICM,6]
	ECLA	A61K031/00+A; A61K031/4045; A61K031/4525 <--

AB Depression and other CNS diseases are treated by enhancing 5-HT2B receptor function with a 5-HT2B agonist or pos. allosteric modulator. The 5-HT2B agonist is e.g. 1-(5-thienylmethoxy-1H-3-indolyl)propan-2-amine (BW 723C86).

ST antidepressant serotoninergic S2B agonist; CNS disease serotoninergic S2B agonist; thienylmethoxyindolylpropanamine antidepressant CNS disease; BW 723C86 antidepressant CNS disease

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT1A; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT1B; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT1D; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT1E; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT1F; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT2A; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Allosterism
Antidepressants
Antimigraine agents
Nervous system agents
(5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(5-HT2B; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT2C; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT4; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT6; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT 5-HT receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(5-HT7; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Dopamine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(D2; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Dopamine receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(D3; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Drugs of abuse
(addiction; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Appetite
(bulimia; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Fatigue, biological
(chronic fatigue syndrome; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Behavior
(conflict, Vogel conflict test; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT **Mental disorder**
(**dementia**, behavior disorder associated with; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of **depression** and other CNS diseases)

IT Behavior

(disorder, dementia-associated; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Stomach
(fundus; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT **Schizophrenia**
(neg. symptoms; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT **Mental disorder**
(**obsession-compulsion**; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of **depression** and other CNS diseases)

IT Anxiety
(panic disorder; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT **Mental disorder**
(**phobia**, social; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of **depression** and other CNS diseases)

IT Ovarian cycle
(premenstrual syndrome; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Behavior
(social, social interaction; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT Drug dependence
(to drugs of abuse; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

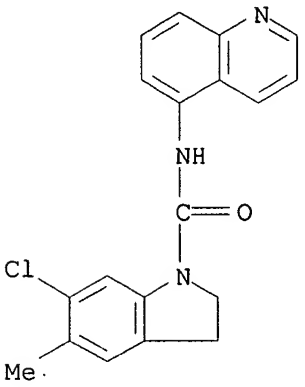
IT Adrenoceptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(α1B; 5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT **162100-15-4**, 6-Chloro-5-methyl-1-(5-quinolylcarbamoyl)indoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

IT **61869-08-7**, **Paroxetine** 160521-72-2, Bw 723c86
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

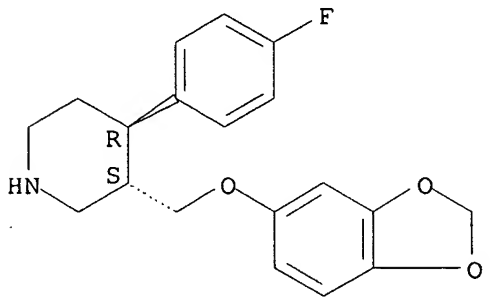
IT **162100-15-4**, 6-Chloro-5-methyl-1-(5-quinolylcarbamoyl)indoline
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)

RN 162100-15-4 HCAPLUS
CN 1H-Indole-1-carboxamide, 6-chloro-2,3-dihydro-5-methyl-N-5-quinolinyl- (9CI) (CA INDEX NAME)



IT **61869-08-7, Paroxetine**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-HT2B receptor function enhancement with 5-HT2B agonist or pos. allosteric modulator for treatment of depression and other CNS diseases)
RN 61869-08-7 HCAPLUS
CN Piperidine, 3-[(1,3-benzodioxol-5-yloxy)methyl]-4-(4-fluorophenyl)-, (3S,4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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L133 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:995776 HCAPLUS
DN 141:406120
ED Entered STN: 19 Nov 2004
TI Compositions and methods for the treatment of parkinson's disease and tardive dyskinesias with quinoline ring-containing neuromelanin-binding compounds
IN **Nelson, Jodi**
PA USA

SO U.S. Pat. Appl. Publ., 24 pp., Cont.-in-part of U.S. Ser. No. 192,414.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-47
INCL 514313000
CC 1-11 (Pharmacology)
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 2004229908	A1	20041118	US 2003-616692	20030709	<--
	US 6417177	B1	20020709	US 2000-615639	20000713	<--
	US 2002198231	A1	20021226			
PRAI	US 1999-143767P	P	19990713			
	US 2000-175051P	P	20000107			
	US 2000-202140P	P	20000505			
	US 2000-615639	A2	20000713			
	US 2002-192414	A2	20020709			
	US 2003-479748P	P	20030619			

applicant

Broader context

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION
US 2004229908	ICM	A61K031-47
	INCL	514313000
	IPCI	A61K0031-47 [ICM,7]
	NCL	514/313.000
	ECLA	A61K031/355+M; A61K031/375+M; A61K031/47+A; A61K031/4706; A61K031/4706+M; A61K047/48R2P; A61K047/48T4B18 <--
US 6417177	IPCI	A61K0031-47 [ICM,7]; A61P0025-16 [ICS,7]
	NCL	514/082.000; 514/007.000; 514/105.000
	ECLA	A61K031/355+M; A61K031/375+M; A61K031/4706; A61K031/4706+M; A61K047/48R2P; A61K047/48T4B18 <--
US 2002198231	IPCI	A61K0031-4706 [ICM,7]
	NCL	514/313.000
	ECLA	A61K031/355+M; A61K031/375+M; A61K031/47+A; A61K031/4706; A61K031/4706+M; A61K047/48R2P; A61K047/48T4B18

AB This invention provides compns. and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration, as well as drug-induced dyskinesias, tardive dyskinesia, Neuroleptic Malignant Syndrome, and neg. symptoms of schizophrenia. An effective amount of a neuromelanin-binding composition having a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-**chloroquine diphosphate**. Selected adjuvants are also provided as part of the compns. of this invention.

ST parkinsonism treatment quinoline analog adjuvant

IT **Nervous system, disease**
(Huntington's **chorea**, movement disorder from; treatment of parkinson's **disease** and **tardive dyskinesias** using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Nervous system, disease**
(**akathisia**, drug-induced; treatment of parkinson's **disease** and **tardive dyskinesias** using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome

P 450 inhibitors and dopamine modulators)
IT Disease, animal
(atrophy, multiple symptom; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT **Neuron**
(catecholaminergic, melanized, reducing apoptosis in; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT **Nervous system, disease**
(**chorea**, drug-induced; treatment of parkinson's **disease** and **tardive dyskinesias** using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT **Brain**
(corpus striatum, glial-derived neurotrophic factor increase in; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT Drug delivery systems
(delayed release; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT **Mental and behavioral disorders**
(depression, in schizophrenia; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT Drug toxicity
(dyskinesia from; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT **Nervous system, disease**
(**extrapyramidal**, drug-induced; treatment of parkinson's **disease** and **tardive dyskinesias** using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT Neurotrophic factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glial-derived, in nigrostriatal neural degeneration; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT **Brain**
(globus pallidus, glial-derived neurotrophic factor increase in; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT **Amnesia**
Cognitive disorders
(in Parkinson's disease; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT Apoptosis
(in melanized catecholaminergic neurons, inhibition; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)
IT Oxidative stress, biological
(inhibition, in schizophrenia; treatment of parkinson's disease and

tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Metabolism, animal**
(inhibitors; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Mental and behavioral disorders**
(lack of motivation, in schizophrenia; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Motor skill disorders**
(motor fluctuations; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Wilson's disease**
(movement disorder from; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Schizophrenia**
(neg. symptoms; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Nervous system, disease**
(**neuroleptic malignant syndrome**; treatment of parkinson's **disease** and **tardive dyskinesias** using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT Melanins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neuromelanins; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT Cytoprotective agents
(neuroprotective, for melanized catecholaminergic neurons; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Brain, disease**
(nigrostriatal **degeneration**, movement disorder from; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Brain**
(substantia nigra, glial-derived neurotrophic factor increase in; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT Drug interactions
(synergistic; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Nervous system, disease**
(**tardive dyskinesia**; treatment of parkinson's **disease** and **tardive dyskinesias** using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Brain, disease**
(thalamic hyperactivity, decrease of; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs

and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **Antiparkinsonian agents**
Antipsychotics
Cognition enhancers
Combination chemotherapy
Dopamine agonists
Dopamine antagonists
Human
Movement disorders
Parkinson's disease
(treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **70458-96-7**, Norfloxacin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Norfloxacinem**; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **329322-82-9**, Cytochrome P 450 3A **330597-62-1**, Cytochrome P 450 2D6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **132-22-9, Chlorpheniramine**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of parkinsons disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT 59-92-7, Levodopa, biological studies
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT **67459-54-5**, (-)-**Chloroquine diphosphate**
69698-55-1, (+)-**Chloroquine diphosphate**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

IT 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies
50-63-5, Chloroquine diphosphate 51-61-6,
Dopamine, biological studies 51-61-6D, Dopamine, precursors, biological studies 52-86-8, Haloperidol **54-05-7**, Chloroquine
56-54-2, Quinidine 58-38-8, Prochlorperazine
58-39-9, Perphenazine 58-40-2, Promazine **60-99-1**,
Levomepromazine 69-23-8, Fluphenazine 113-59-7,
Chlorprothixene **114-07-8, Erythromycin** 117-89-5,
Trifluoperazine **118-42-3**, Hydroxychloroquine **134-31-6**,
8-Quinolinol sulfate **147-84-2**, biological studies
303-49-1, Clomipramine 364-62-5,
Metoclopramide 442-96-6 1915-92-0
1951-25-3, Amiodarone 1977-10-2, Loxapine 2062-78-4,
Pimozide 2739-16-4, 3,4-Dihydro-1-(2H)-quinolinecarboxaldehyde
3313-26-6, Thiothixene 4169-19-1, 1-Acetyl-1,2,3,4-tetrahydroquinoline

5002-47-1, Fluphenazine decanoate 5588-33-0, Mesoridazine
6168-85-0 7416-34-4, Molindone 24283-71-4,
1-Butyryl-1,2,3,4-tetrahydroquinoline **32571-37-2 42399-41-7**
, Diltiazem 51481-61-9, Cimetidine
53462-15-0 54739-18-3, Fluvoxamine
54910-89-3, Fluoxetine 61869-08-7,
Paroxetine 65277-42-1, Ketoconazole
66357-35-5, Ranitidine 71320-77-9,
Moclobemide 74050-97-8, Haloperidol decanoate **79617-96-2**
, Sertraline 81103-11-9, Clarithromycin
83366-66-9, Nefazodone 83891-03-6,
Norfluoxetine 84371-65-3, Mifepristone
84625-61-6, Itraconazole 85721-33-1,
Ciprofloxacin 86166-07-6 86386-73-4,
Fluconazole 91161-71-6, Terbinafine
99218-67-4 116644-53-2, Mibefradil
127779-20-8, Saquinavir 136817-59-9,
Delavirdine 150378-17-9, Indinavir
155213-67-5, Ritonavir 159989-64-7,
Nelfinavir 169590-42-5, Celecoxib
319912-96-4 319912-97-5 319912-98-6
319913-01-4 319913-02-5 319913-03-6
319913-04-7 319913-05-8 319913-08-1
478784-57-5 478784-58-6 478784-60-0
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478784-67-7 478784-68-8 478784-70-2
478784-71-3 645406-28-6 645406-30-0
645406-32-2 645406-38-8 645406-39-9
645406-40-2 645406-41-3 645406-46-8
645406-47-9 645406-48-0 645406-49-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of parkinson's disease and tardive dyskinesias using neuromelanin-binding quinoline analogs and adjuvants such as cytochrome P 450 inhibitors and dopamine modulators)

L133 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:41228 HCAPLUS
DN 140:105304
ED Entered STN: 18 Jan 2004
TI Compositions and methods for the treatment of Parkinson's disease and tardive dyskinesias
IN **Nelson, Jodi**
PA **Alpha Research Group, L.L.C., USA**
SO PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004004660	A2	20040115	WO 2003-US21463	20030709 <--
WO 2004004660	A3	20051103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,

PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002198231 A1 20021226 US 2002-192414 20020709
EP 1581167 A2 20051005 EP 2003-763398 20030709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 2002-192414 A 20020709
US 2003-479748P P 20030619
US 1999-143767P P 19990713
US 2000-175051P P 20000107
US 2000-202140P P 20000505
US 2000-615639 A2 20000713
WO 2003-US21463 W 20030709

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004004660	ICM	A61K
	IPCI	A61K [ICM,7]; A61K0031-47 [ICS,7]
	ECLA	A61K031/355+M; A61K031/375+M; A61K031/47+A; A61K031/4706; A61K031/4706+M <--
US 2002198231	IPCI	A61K0031-4706 [ICM,7]
	NCL	514/313.000
	ECLA	A61K031/355+M; A61K031/375+M; A61K031/47+A; A61K031/4706; A61K031/4706+M; A61K047/48R2P; A61K047/48T4B18
EP 1581167	IPCI	A61K0007-00 [ICM,7]
	ECLA	A61K031/355+M; A61K031/375+M; A61K031/47+A; A61K031/4706; A61K031/4706+M

AB This invention provides compns. and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration, as well as drug-induced dyskinesias, tardive dyskinesia, Neuroleptic Malignant Syndrome, and neg. symptoms of schizophrenia. An effective amount of a neuromelanin-binding composition having a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-**chloroquine diphosphate**. Selected adjuvants are also provided as part of the compns. of this invention.

ST chloroquine catecholamine neuron respiration Parkinson disease tardive dyskinesia therapy

IT Antihistamines
(H1; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT Lactoferrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibodies; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Neuron**
(catecholaminergic, melanized; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT Antioxidants
Antiparkinsonian agents
Dopamine agonists
Dopamine antagonists

Drug delivery systems
Human
Motor skill disorders
Respiration, animal
Schizophrenia
(compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT Drug delivery systems
(controlled-release, time; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Brain**
(corpus striatum; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Nerve, disease**
(**degeneration**, striatal; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Cognitive disorders**
(from Parkinson's disease; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT Neurotrophic factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glial-derived; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Brain**
(globus pallidus; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(lactoferrins; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Parkinson's disease**
(multiple symptom atrophy associated with, plus syndrome, atypical; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Nervous system, disease**
(**neuroleptic malignant syndrome**; compns. for treatment of Parkinson's **disease** and **tardive dyskinesias**)

IT Cytoprotective agents
(peripheral membrane, retinal; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Brain**
(substantia nigra; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **Nervous system, disease**
(**tardive dyskinesia**; compns. for treatment of Parkinson's **disease** and **tardive dyskinesias**)

IT **Hyperkinesia**
(thalamic; compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT **329322-82-9**, Cytochrome P450 3A **330597-62-1**, Cytochrome P450 2D6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT 50-52-2, Thioridazine 50-53-3, Chlorpromazine, biological studies **50-63-5**, **Chloroquine phosphate** 50-81-7, Vitamin C, biological studies 52-86-8, Haloperidol **54-05-7**, Chloroquine **56-54-2**, **Quinidine** 58-33-3, Promethazine hydrochloride 58-38-8, Prochlorperazine 58-39-9, Perphenazine 58-40-2, Promazine 58-73-1, Diphenhydramine 59-33-6, Pyrilamine maleate **60-99-1**, **Levomepromazine** 69-23-8,

Fluphenazine 73-31-4, Melatonin 91-81-6, Tripelennamine 113-59-7, Chlorprothixene **113-92-8 114-07-8**, **Erythromycin** 117-89-5, Trifluoperazine **118-42-3**, Hydroxychloroquine 128-37-0, Butylated hydroxytoluene, biological studies **147-84-2**, biological studies 299-28-5, Calcium gluconate 303-25-3, Cyclizine hydrochloride **303-49-1**, **Clomipramine 364-62-5**, **Metoclopramide 442-96-6** 523-87-5, Dimenhydrinate 814-80-2, Calcium lactate 980-71-2, Brompheniramine maleate 1104-22-9, Meclizine hydrochloride 1244-76-4 1406-16-2, Vitamin D 1406-18-4, Vitamin E **1915-92-0 1951-25-3**, **Amiodarone** 1977-10-2, Loxapine 2062-78-4, Pimozide **2149-36-2**, 8-Quinolinol sulfate 2739-16-4 3313-26-6, Thiothixene 3505-38-2, Carbinoxamine maleate 4169-19-1, 1-Acetyl-1,2,3,4-tetrahydroquinoline 5002-47-1, Fluphenazine decanoate 5588-33-0, Mesoridazine 5897-19-8, Cyclizine lactate 7416-34-4, Molindone 7693-13-2, Calcium citrate 9054-89-1, Superoxide dismutase 10103-46-5, Calcium phosphate 10246-75-0, Hydroxyzine pamoate 15686-51-8, Clemastine 23288-49-5, Probucol 24283-71-4, 1-Butyryl-1,2,3,4-tetrahydroquinoline 25013-16-5, Butylated hydroxyanisole **42399-41-7**, **Diltiazem** 50679-08-8, Terfenadine **51050-49-8 51481-61-9**, **Cimetidine 53462-15-0 53462-16-1 54739-18-3**, **Fluvoxamine 54910-89-3**, **Fluoxetine 58175-86-3 58175-87-4 61869-08-7**, **Paroxetine 65277-42-1**, **Ketoconazole 66357-35-5**, **Ranitidine 67459-54-5**, (-)-**Chloroquine diphosphate** 68844-77-9, Astemizole **69698-55-1**, (+)-**Chloroquine diphosphate 70458-96-7**, Norfloxacin **71320-77-9**, **Moclobemide** 74050-97-8, Haloperidol decanoate **79617-96-2**, **Sertraline** 79794-75-5, Loratadine **81103-11-9**, **Clarithromycin 83366-66-9**, **Nefazodone** 83881-52-1, Cetirizine hydrochloride **83891-03-6**, **Norfluoxetine 84371-65-3**, **Mifepristone 84625-61-6**, **Itraconazole 85721-33-1**, **Ciprofloxacin 86386-73-4**, **Fluconazole** 87848-99-5, Acrivastine **91161-71-6**, **Terbinafine 99218-67-4 116644-53-2**, **Mibefradil 127779-20-8**, **Saquinavir 136817-59-9**, **Delavirdine 137433-23-9 137433-24-0 150378-17-9**, **Indinavir 155213-67-5**, **Ritonavir 159989-64-7**, **Nelfinavir 169590-42-5**, **Celecoxib** 174882-69-0, Pycnogenol **319912-96-4 319912-97-5 319912-98-6 319912-99-7 319913-00-3 319913-01-4 319913-02-5 319913-03-6 319913-04-7 319913-05-8 319913-06-9 319913-07-0 319913-08-1 478784-57-5 478784-58-6 478784-60-0 478784-61-1 478784-63-3 478784-64-4 478784-65-5 478784-66-6 478784-67-7 478784-68-8 478784-70-2 478784-71-3 478784-73-5 478784-74-6 645406-19-5 645406-20-8 645406-21-9 645406-22-0 645406-23-1 645406-24-2 645406-25-3 645406-26-4 645406-27-5 645406-29-7 645406-31-1 645406-33-3 645406-34-4 645406-35-5 645406-36-6 645406-38-8 645406-39-9 645406-40-2 645406-41-3 645406-42-4 645406-43-5 645406-44-6 645406-45-7 645406-46-8 645406-47-9**

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645407-11-0 645407-12-1 645407-13-2
645407-15-4 645407-16-5 645407-17-6
645407-18-7 645407-19-8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for treatment of Parkinson's disease and tardive dyskinesias)

IT 51-61-6, Dopamine, biological studies 7440-70-2, Calcium, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. for treatment of Parkinson's disease and tardive dyskinesias)

L133 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:978470 HCAPLUS
DN 138:33365
ED Entered STN: 29 Dec 2002
TI Compositions and methods for the treatment of Parkinson's disease with quinoline ring-containing neuromelanin-binding compounds
IN **Nelson, Jodi**
PA USA
SO U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. 6,417,177.
CODEN: USXXCO
DT Patent
LA English
IC ICM A61K031-4706
INCL 514313000
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2002198231	A1	20021226	US 2002-192414	20020709
US 6417177	B1	20020709	US 2000-615639	20000713 <--
WO 2004004660	A2	20040115	WO 2003-US21463	20030709 <--
WO 2004004660	A3	20051103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,

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            KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
            FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
            BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 2004229908        A1    20041118    US 2003-616692         20030709 <--
     EP 1581167           A2    20051005    EP 2003-763398         20030709
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 1999-143767P      P     19990713
     US 2000-175051P      P     20000107
     US 2000-202140P      P     20000505
     US 2000-615639       A2    20000713
     US 2002-192414       A     20020709
     US 2003-479748P      P     20030619
     WO 2003-US21463      W     20030709
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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 US 2002198231   ICM    A61K031-4706
                 INCL   514313000
                 IPCI   A61K0031-4706 [ICM,7]
                 NCL    514/313.000
                 ECLA   A61K031/355+M; A61K031/375+M; A61K031/47+A;
                        A61K031/4706; A61K031/4706+M; A61K047/48R2P;
                        A61K047/48T4B18
 US 6417177      IPCI   A61K0031-47 [ICM,7]; A61P0025-16 [ICS,7]
                 NCL    514/082.000; 514/007.000; 514/105.000
                 ECLA   A61K031/355+M; A61K031/375+M; A61K031/4706;
                        A61K031/4706+M; A61K047/48R2P; A61K047/48T4B18      <--
 WO 2004004660   IPCI   A61K [ICM,7]; A61K0031-47 [ICS,7]
                 ECLA   A61K031/355+M; A61K031/375+M; A61K031/47+A;
                        A61K031/4706; A61K031/4706+M                        <--
 US 2004229908   IPCI   A61K0031-47 [ICM,7]
                 NCL    514/313.000
                 ECLA   A61K031/355+M; A61K031/375+M; A61K031/47+A;
                        A61K031/4706; A61K031/4706+M; A61K047/48R2P;
                        A61K047/48T4B18                                     <--
 EP 1581167      IPCI   A61K0007-00 [ICM,7]
                 ECLA   A61K031/355+M; A61K031/375+M; A61K031/47+A;
                        A61K031/4706; A61K031/4706+M
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AB This invention provides compns. and methods for increasing cellular respiration of melanized catecholamine neurons, and methods for alleviating symptoms or stopping appearance and/or progression of symptoms of Parkinson's disease and related conditions, characterized by nigrostriatal degeneration. An effective amount of a neuromelanin-binding composition having a quinoline ring in a suitable pharmaceutical carrier is administered to patient in need of such treatment. Preferably the composition comprises (-)-chloroquine. Selected adjuvants are also provided as part of the compns. of this invention.

ST Parkinson disease treatment chloroquine compd; antiparkinsonian quinoline ring contg neuromelanin binding compd; melanized catecholamine neuron respiration chloroquine compd

IT Antihistamines
(H1, enhancing agent adjuvant; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **Brain**
(adjuvant targeting; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Antioxidants
Dopamine agonists
Radical scavengers

(adjuvant; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Lactoferrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antibody to, conjugates with chloroquine compound; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **Neuron**
(catecholaminergic, increasing cellular respiration of melanized; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Lipophilicity
(chloroquine compound conjugates with agent having; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Antibodies and Immunoglobulins
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjugates, with chloroquine compound, to lactotransferrin; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Respiration, animal
(enhancement of melanized catecholamine neurons; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Drug delivery systems
(immunoconjugates, anti-lactotransferrin antibody conjugates with chloroquine compound; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **Nervous system, disease**
(**multiple system atrophy**; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's **disease**)

IT Melanins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neuromelanins, quinoline ring-containing compound binding to; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Cytoprotective agents
(neuroprotective, adjuvant; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **Brain, disease**
(nigrostriatal **degeneration**; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **Metabolism, animal**
(peripheral, inhibitor of; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Cell membrane
(protective agent as adjuvant; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **Antiparkinsonian agents**
Cognition enhancers
Drug delivery systems
Enantiomers
Human
Parkinson's disease
(quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Salts, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Mixtures
(racemic; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Eye
(retina, protective agent as adjuvant; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT Drug delivery systems
(timed-release; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT 51-61-6, Dopamine, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT 50-81-7, Vitamin C, biological studies 73-31-4, Melatonin 128-37-0, Butylated hydroxytoluene, biological studies 1406-18-4, Vitamin E 9054-89-1, Superoxide dismutase 23288-49-5, Probucol 25013-16-5, Butylated hydroxyanisole 174882-69-0, Pycnogenol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antioxidant adjuvant; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT 299-28-5, Calcium gluconate 814-80-2, Calcium lactate 1406-16-2, Vitamin D 7693-13-2, Calcium citrate 10103-46-5, Calcium phosphate 14127-61-8, Calcium ion, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as peripheral membrane protective agent; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **1951-25-3, Amiodarone 51481-61-9, Cimetidine**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytochrome P 450 2D6 and A3 inhibitor inhibiting peripheral metabolism of chloroquine compds.; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **56-54-2, Quinidine 60-99-1, Levomepromazine 303-49-1, Clomipramine 364-62-5, Metoclopramide 54910-89-3, Fluoxetine 61869-08-7, Paroxetine 66357-35-5, Ranitidine 71320-77-9, Moclobemide 79617-96-2, Sertraline 91161-71-6, Terbinafine 116644-53-2, Mibefradil 155213-67-5, Ritonavir 169590-42-5, Celecoxib**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytochrome P 450 2D6 inhibitor inhibiting peripheral metabolism of chloroquine compds.; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **114-07-8, Erythromycin 147-84-2**, biological studies **42399-41-7, Diltiazem 54739-18-3, Fluvoxamine 65277-42-1, Ketoconazole 70458-96-7**, Norfloxacin **81103-11-9, Clarithromycin 83366-66-9, Nefazodone 83891-03-6, Norfluoxetine 84371-65-3, Mifepristone 84625-61-6, Itraconazole 85721-33-1, Ciprofloxacin 86386-73-4, Fluconazole 127779-20-8, Saquinavir**

136817-59-9, Delavirdine 150378-17-9,
Indinavir 159989-64-7, Nelfinavir
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytochrome P 450 A3 inhibitor inhibiting peripheral metabolism of chloroquine compds.; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT 58-33-3, Promethazine hydrochloride 58-73-1, Diphenhydramine 59-33-6, Pyrilamine maleate 91-81-6, Tripelenamine **113-92-8,**
Chlorpheniramine maleate 303-25-3, Cyclizine hydrochloride
523-87-5, Dimenhydrinate 980-71-2, Brompheniramine maleate 1104-22-9, Meclizine hydrochloride 2192-20-3, Hydroxyzine hydrochloride
3505-38-2, Carbinoxamine maleate 5897-19-8, Cyclizine lactate
10246-75-0, Hydroxyzine pamoate 15686-51-8, Clemastine 50679-08-8, Terfenadine 68844-77-9, Astemizole 79794-75-5, Loratadine
83881-52-1, Cetirizine hydrochloride 87848-99-5, Acrivastine
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(histamine H1 receptor antagonist as enhancing agent adjuvant; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **329322-82-9,** Cytochrome P450 3A **330597-62-1,** Cytochrome P450 2D6
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor of; quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

IT **50-63-5, Chloroquine phosphate 54-05-7**
, Chloroquine **118-42-3,** Hydroxychloroquine **134-31-6,**
8-Quinolinol sulfate **442-96-6 1915-92-0** 2739-16-4
4169-19-1, 1-Acetyl-1,2,3,4-tetrahydroquinoline **4298-15-1**
6168-85-0 24283-71-4, 1-Butyryl-1,2,3,4-tetrahydroquinoline
32571-37-2 53462-15-0 58175-87-4,
(-)-Chloroquine **82351-01-7 99218-67-4**
319912-96-4 319912-97-5 319912-98-6
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319913-06-9 319913-07-0 319913-08-1
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478784-65-5 478784-66-6 478784-67-7
478784-68-8 478784-70-2 478784-71-3
478784-73-5 478784-74-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinoline ring-containing neuromelanin-binding compds. for treatment of Parkinson's disease)

L133 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2000:68339 HCAPLUS
DN 132:117553
ED Entered STN: 28 Jan 2000
TI Treatment for schizophrenia and other dopamine system dysfunctions using MPTP and analogs
IN **Nelson, Jodi A.**
PA USA
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-44

CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000003713	A1	20000127	WO 1999-US15961	19990714
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9949959	A1	20000207	AU 1999-49959	19990714
PRAI	US 1998-92792P	P	19980714		
	US 1999-232311	A	19990115		
	WO 1999-US15961	W	19990714		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000003713	ICM	A61K031-44
	IPCI	A61K0031-44 [ICM,6]
	ECLA	A61K031/44+A; A61K031/44+M; A61K031/4418; A61K031/4425; A61K031/443; A61K031/4436; A61K045/06+M
AU 9949959	IPCI	A61K0031-44 [ICM,6]

OS MARPAT 132:117553

AB Methods and compns. containing 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) and its analogs and/or pyridinium ions thereof for the treatment of pos. and neg. symptoms of schizophrenia and tardive dyskinesia are provided. Compns. are administered in amts. sufficient to reduce dopamine levels in subcortical areas of the brain without causing symptoms of Parkinson's disease. One course of treatment can result in permanent or long-term amelioration of symptoms. Selective neuroprotective agents, neurotoxicity-enhancing agents, and dopamine upregulation agents or other antidote may be administered in combination with MPTP and analogs as part of the treatment. For example, i.p. administration of neurotoxic MPTP (5, 10, and 15 mg/kg) to mice, combined with a neurotoxicity-enhancing agent (acetaldehyde, 250 mg/kg 10 min prior and 20 min following the administration of MPTP) for 5 consecutive days produced a dopamine depletion which was repotentiated by administration of a neuroprotectant, deprenyl (0.25 mg/kg).

ST MPTP analog neurotoxin dopamine neuron schizophrenia; pyridine tetrahydromethylphenyl antipsychotic schizophrenia tardive dyskinesia

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with; compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia)

IT Antipsychotics
Drug delivery systems
Schizophrenia
(compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia)

IT **Nerve**
(**dopaminergic**; compns. containing MPTP or analogs as neurotoxins for dopamine **neurons** for treatment of schizophrenia and tardive dyskinesia)

IT Melanins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(neuromelanins, compds. with affinity for, combination with; compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia)
IT Cytoprotective agents
(neuroprotectants, combination with; compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia)
IT **Nervous system**
(**tardive dyskinesia**; compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and **tardive dyskinesia**)
IT 9001-66-5, Monoamine oxidase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A and B; compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia in combination with MAO inhibitors)
IT 50-47-5, Desipramine **54-05-7**, Chloroquine 55-65-2, Guanethidine 2323-36-6, Deprenyl 2942-42-9, 7-Nitroindazole 14611-51-9, Selegiline 56862-28-3 59729-33-8, Citalopram 77086-22-7, MK 801
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination with; compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia)
IT 13458-14-5 28289-54-5, 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine 48134-75-4 57070-49-2 75663-55-7 102417-86-7 115900-05-5 115900-06-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia)
IT 51-61-6, Dopamine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia)
IT 75-07-0, Acetaldehyde, biological studies **147-84-2**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neurotoxicity-enhancing agent, combination with; compns. containing MPTP or analogs as neurotoxins for dopamine neurons for treatment of schizophrenia and tardive dyskinesia)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bymaster; US 5750541 A 1998 HCAPLUS
(2) Fredriksson, A; Journal of Neural Transmission 1995, V102, P19 HCAPLUS
(3) Godel; US 5688798 A 1997 HCAPLUS
(4) Mytilineou, C; Journal of Neurochemistry 1985, V45(6), P1951 HCAPLUS

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FILE 'WPIX' ENTERED AT 09:27:11 ON 21 DEC 2005

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http://www.stn-international.de/stndatabases/details/ipc_reform.html <
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L175 ANSWER 1 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2004-214263 [20] WPIX
CR 2001-147126 [15]
DNC C2004-084759
TI Composition useful for treating e.g. motor fluctuations and multiple symptom atrophy associated with **Parkinson**'s disease comprises neuromelanin-binding agent e.g. chloroquine.
DC B02 B05
IN **NELSON, J**
PA (ALPH-N) ALPHA RES GROUP LLC; (NELS-I) NELSON J
CYC 103
PI WO 2004004660 A2 20040115 (200420)* EN 52 A61K000-00
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
AU 2003248893 A1 20040123 (200459) A61K000-00
US 2004229908 A1 20041118 (200477) A61K031-47 <--
EP 1581167 A2 20051005 (200565) EN A61K007-00
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
ADT WO 2004004660 A2 WO 2003-US21463 20030709; AU 2003248893 A1 AU 2003-248893 20030709; US 2004229908 A1 Provisional US 1999-143767P 19990713, Provisional US 2000-175051P 20000107, Provisional US 2000-202140P 20000505, CIP of US 2000-615639 20000713, CIP of US 2002-192414 20020709,

Provisional US 2003-479748P 20030619, US 2003-616692 20030709; EP 1581167 A2 EP 2003-763398 20030709, WO 2003-US21463 20030709

FDT AU 2003248893 A1 Based on WO 2004004660; US 2004229908 A1 CIP of US 6417177; EP 1581167 A2 Based on WO 2004004660

PRAI US 2003-479748P 20030619; US 2002-192414 20020709;
US 1999-143767P 19990713; US 2000-175051P 20000107;
US 2000-202140P 20000505; US 2000-615639 20000713;
US 2003-616692 20030709

IC ICM A61K000-00; A61K007-00; **A61K031-47**

AB WO2004004660 A UPAB: 20051011

NOVELTY - A composition (C1) comprising neuromelanin-binding agent (I) selected from 45 compounds as given in the specification, e.g. chloroquine, its fluorine analogs, or derivatives containing quinoline nucleus including 7-fluoro-4-(4-diethylamino-1-methylbutylamino)quinoline and **chloroquine phosphate**, and/or their salts complexed, covalently linked or mixed with an adjuvant, is new.

ACTIVITY - Tranquilizer; **Antiparkinsonian**; Nootropic; Muscular-Gen.; Neuroleptic.

The neuroprotective activity of **chloroquine diphosphate** was evaluated in the patients diagnosed with multiple symptom atrophy. Initially patients were administered with a test medication (155 mg) comprising chloroquine and **cimetidine**, 4 times a day. The medication was administered at a dosage of: 155 mg/thrice a day on days 2 and 3; 155 mg/twice a day on days 4 - 6; and 155 mg/day on day 7 onward. After 14 days of the treatment, functional evaluations by Unified **Parkinson**'s Disease Rating scale (UPDRS) were made. The UPDRS scores after 14 days/baseline were 82/85. The patient's speech therapist and physical therapist reported significant improvement in speech and range of motion.

MECHANISM OF ACTION - Melanized Catecholamine Neuronal Respiration Enhancer.

USE - The composition is useful for reducing the amount of dopamine or dopamine agonist; for inhibiting oxidative stress responsible for negative symptoms of **schizophrenia**; for reducing apoptosis and increasing cellular respiration in melanized catecholamine neurons; for selectively increasing glial-derived neurotrophic factor (GDNF) in the substantia nigra, striatum and/or globus pallidus; for reducing thalamic hyperactivity; and for treating idiopathic **Parkinson**'s disease, multiple symptom atrophy associated with **Parkinson**'s disease, **Parkinson**'s plus syndrome, atypical **Parkinsonian** disorder, cognitive symptoms of **Parkinson**'s disease, on-off syndrome associated with dopamine or dopamine agonist, vascular **Parkinson**'s disease, drug-induced **dyskinesias**, tardive **dyskinesias**, motor fluctuation, neuroleptic malignant syndrome, and negative symptoms of **schizophrenia**) (all claimed).

ADVANTAGE - The composition reduces the amount of dopamine or dopamine agonist used in the treatment of e.g. **Parkinson**'s disease, and hence reduces or prevents syndromes or side effects associated with the treatment. The composition effectively improves cognition, alleviates motor symptoms, and attenuates progression of **Parkinson**'s disease.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B01-C05; B02-E; B06-A01; B06-A02; B06-B02; B06-D01; B06-D02; B06-D03; B06-D04; B06-D05; B06-D12; B06-E05; B06-F03; B06-F04; B07-A01; B07-A02B; B07-A03; B07-A04; B07-D03; B07-D04C; B07-D05; B07-D08; B07-D09; B07-D11; B07-D13; B07-E03; B07-F01; B10-A11A; B10-A18; B10-B01A; B10-B03B; B10-B04B; B10-C02; B14-H04; **B14-J01A3**; B14-J01A4; **B14-J01B3**; B14-J02D3; **B14-J05**;

B14-L01; B14-L06; B14-L09
TECH UPTX: 20040324
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Composition: (C1) Comprises (I) (100 - 500, preferably 100 - 200 mg), calcium ion (1000 - 2000 mg) and vitamin D (700 - 900 IU). (C1) Further comprises a second active ingredient. (C1) Is in the form of a time-release preparation, and the **peripheral** protective agent is not complexed or covalently bound to (I). (C1) Releases the **peripheral** protective agent from 1.5 - 3 hours prior to release of (I); **peripheral metabolism** inhibitor from 1.5 - 2 hours after the **peripheral** protective agent and 1 hour before (I); or first- and second-generation histamine H1 receptor concurrently with (I). (I) Is covalently linked to a lactotransferrin antibody or with a lipophilic moiety. (I) Consist of a (-)-enantiomer, and a lesser amount of (+)-enantiomer (0 - 20%) of the total enantiomeric mixture. The ratio of (I) to dopamine or its agonist is 5:95 - 25:75.
Preferred Components: The adjuvant is **peripheral** membrane protective agent (preferably retinal protective agent), enhancing agent (preferably histamine H1 receptor antagonist, especially first-/second-generation histamine H1 receptor antagonist), **peripheral metabolism** inhibitor (preferably inhibitors of cytochrome P450 2D6 and/or 3A enzyme), neural protective compound other than (I), dopamine or its agonist, free radical deactivator, antioxidant (preferably probucol, pycnogenol, vitamin C, vitamin E, butylated hydroxytoluene, butylated hydroxyanisole (BHA), melatonin or superoxide dismutase) or brain-targeting agent. The second active ingredient is dopamine, dopamine precursor, dopamine agonist or dopamine antagonist. (I) Is chloroquine, **chloroquine phosphate**, hydroxychloroquine, their racemic mixture or enantiomers, covalently linked, mixed, or complexed with an adjuvant, or its salt or mixture. The **peripheral** protective agent is calcium citrate, calcium gluconate, calcium lactate or calcium phosphate, or vitamin D). The cytochrome (CYP) 2D6 enzyme inhibitor is **amiodarone, celecoxib, chlorpheniramine, cimetidine, clomipramine, fluoxetine, levomepromazine, metoclopramide, mibefradil, moclobemide, paroxetine, quinidine, ranitidine, ritonavir, sertraline, terbinafine**, their racemic mixture, enantiomers or salts (preferably **amiodarone, cimetidine** or their salts). The cytochrome P450 3A enzyme inhibitor is **delavirdine, indinavir, nelfinavir, saquinavir, amiodarone, cimetidine, ciprofloxacin, clarithromycin, diethyl-dithiocarbamate, diltiazem, erythromycin, fluconazole, fluvoxamine, itraconazole, ketoconazole, mifepristone, nefazodone**, norfloxacin, **norfluoxetine**, their racemic mixture, enantiomers or salts. The first generation histamine H1 receptor antagonist is carbinoxamine maleate, clemastine, diphenhydramine, dimenhydrinate, pyrilamine maleate, tripelennamine, **chlorpheniramine** maleate, brompheniramine maleate, hydroxyzine hydrochloride, hydroxyzine pamoate, cyclizine hydrochloride, cyclizine lactate, meclizine hydrochloride, promethazine hydrochloride, their racemic mixture, enantiomers or salts. The second-generation histamine H1 receptor antagonist is acrivastine, cetirizine hydrochloride, astemizole, loratadine, terfenadine, their racemic mixture, enantiomers or salts. The dopamine antagonist is chlorpromazine, chlorprothixene, fluphenazine, haloperidol, loxapine, mesoridazine, molindone, perphenazine, pimozide, prochlorperazine, promazine, thioridazine, thiothixene, trifluoperazine, fluphenazine decanoate or haloperidol decanoate.

ABEX UPTX: 20040324
ADMINISTRATION - Dosage of (I) is 0.5 - 1000 mg/day, and administered orally or parenterally (e.g. intravenously, intramuscularly, subcutaneously or intraperitoneally).

EXAMPLE - No suitable example given.

L175 ANSWER 2 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2003-865405 [80] WPIX
DNC C2003-244776
TI Use of zinc ionophoric material, capable of delivering excess zinc across a cellular membrane to inhibit eukaryotic cell metabolism, for treating microbial and fungal infections and dandruff.
DC B05 C03
IN GAVIN, D F; KAUFMAN, D J; MARGRAF, C H; MARSH, R G; **NELSON, J D**; POLSON, G; ROBERTS, K P; SCHWARTZ, J R; TURLEY, P A; POISON, G
PA (PROC) PROCTER & GAMBLE CO; (ARCH-N) ARCH CHEM; (PROC) PROCTER & GAMBLE; (ARCH-N) ARCH CHEM INC; (GAVI-I) GAVIN D F; (KAU MARGRAF C H; (MARS-I) MARSH R G; (NELS-I) NELSON (ROBE-I) ROBERTS K P; (SCHW-I) SCHWARTZ J R; (TU
CYC 103
PI WO 2003088965 A1 20031030 (200380)* EN 62
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GI LU MC MW MZ NL OA PT RO SD SE SI SK SL SI
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA DM DZ EC EE ES FI GB GD GE GH GM HR HU ID KZ LC LK LR LS LT LU LV MA MD MG MK MN MW PT RO RU SC SD SE SG SK SL TJ TM TN TR TT
US 2004058855 A1 20040325 (200422)
AU 2003218279 A1 20031103 (200438)
EP 1496899 A1 20050119 (200506) EN A61K031-44
R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR
JP 2005526111 W 20050902 (200559) 53 A61K031-44
CN 1646124 A 20050727 (200580) A61K031-44
ADT WO 2003088965 A1 WO 2003-US8476 20030318; US 2004058855 A1 Provisional US 2002-374347P 20020422, US 2003-392104 20030318; AU 2003218279 A1 AU 2003-218279 20030318; EP 1496899 A1 EP 2003-714273 20030318, WO 2003-US8476 20030318; JP 2005526111 W JP 2003-585717 20030318, WO 2003-US8476 20030318; CN 1646124 A CN 2003-808988 20030318
FDT AU 2003218279 A1 Based on WO 2003088965; EP 1496899 A1 Based on WO 2003088965; JP 2005526111 W Based on WO 2003088965
PRAI US 2002-374347P 20020422; US 2003-392104 20030318
IC ICM A61K031-44; A61K038-16
ICS A61K007-00; A61K007-06; A61K007-075; A61K007-40; A61K031-145; A61K031-27; A61K031-28; A61K031-315; A61K031-351; A61K031-423; **A61K031-47**; A61K031-555; A61K033-30; A61P017-00; A61P031-00; A61P031-02; A61P031-10; A61P043-00
AB WO2003088965 A UPAB: 20031211
NOVELTY - Delivery of excess zinc to eukaryotic cells to inhibit the cell metabolism comprises treating the cells with a zinc ionophoric material (I) (having a minimum inhibitory concentration (MIC) of less than 500 ppm) that is capable of delivering a zinc ion across a cellular membrane.
ACTIVITY - Fungicide; Antifungal; Antidandruff.
MECHANISM OF ACTION - Eukaryotic cell metabolism inhibitor.
USE - Compositions comprising (I) are useful in the treatment of microbial infections, fungal infections and dandruff (claimed). They are useful for cleansing skin and hair and controlling a variety of microbial infections on the skin or scalp, in animals as well as humans. Such infections include tinea pedis, onychomycosis, yeast infections and diaper

false hit

rash.

ADVANTAGE - Compositions comprising (I) are physically stable and provide improved anti-dandruff efficacy due to the use of materials exhibiting zinc ionophoric behavior.

Dwg.0/0

FS CPI

FA AB; DCN

MC CPI: B02-A; B02-C01; B02-I; B03-G; B04-N02; B04-N04; B05-A01B; B05-A03A; B05-B02A3; B05-B02C; B05-C04; B05-C07; B06-D02; B07-A02A; B07-A02B; B07-A03; B07-D04C; B07-D04D; B07-D09; B10-A04; B10-A12A; B10-C04E; B14-A01; B14-A04; B14-A04C; B14-L06; B14-N17; B14-R02; C02-A; C02-C01; C02-I; C03-G; C04-N02; C04-N04; C05-A01B; C05-A03A; C05-B02A3; C05-B02C; C05-C04; C05-C07; C06-D02; C07-A02A; C07-A02B; C07-A03; C07-D04C; C07-D04D; C07-D09; C10-A04; C10-A12A; C10-C04E; C14-A01; C14-A04; C14-A04C; C14-L06; C14-N17; C14-R02

TECH UPTX: 20031211

TECHNOLOGY FOCUS - ORGANIC CHEMISTRY - Preferred Process: The delivery of excess zinc to the cells takes place when (I) is in combination with a zinc containing material (II), resulting in a 1.5 fold (preferably 2.5 fold) increase in intracellular zinc level over that which would occur in the absence of (I). The combination demonstrates an increase in zinc transport that enhances antifungal activity. In the presence of 5 ppm or less of (II), the increase in the antifungal activity of (I) is achieved with at least 50% reduction in the amount of (I) necessary to inhibit cell growth. The process involves reaction of (II) with a metallochromic dye zincon to give a color change from orange to blue.

Preferred Composition: (I) is a zinc salt of the zinc ionophoric material. (I) may be polyvalent metal salts of pyrithiones i.e. pyrithione or a zinc salt of pyrithione (preferably zinc pyrithione), dithiocarbamates (pyrrolidine dithiocarbamate, **diethyldithiocarbamate**, zinc **diethyldithiocarbamate**, disulfiram, dimethyldithiocarbamate and/or zinc dimethyldithiocarbamate), heterocyclic amines (preferably 8-hydroxyquinoline, 5,7-diiodo-8-hydroxyquinoline, 5,7-dichloro-8-hydroxyquinoline, 5-chloro-7-iodo-8-hydroxyquinoline, chloroquinaldol, 2-methyl-5,7-dichloro-8-hydroxyquinoline and/or 5-7-dibromo-8-hydroxyquinoline), nonsteroidal anti-inflammatory compounds, naturally occurring materials having zinc ionophoric behavior and their derivatives, bio-molecules and peptides (preferably lasalocid (X537A), A23187 (calcimycin), 4-BR A23187, ionomycin and/or cyclosporin A), sulfur-based compounds (preferably tetra-n-butyl thiuram disulfide) and transport enhancers (preferably albumin, histidine, arachidonic acid, picolinic acid, dihydroxyvitamin D3 and/or ethylmaltol). (II) is an inorganic material, particularly zinc aluminate, zinc carbonate, zinc oxide, calamine, zinc phosphate, zinc selenide, zinc sulfide, zinc silicates, zinc silicofluoride, zinc borate, zinc-containing layered material and/or zinc hydroxide and zinc hydroxy sulfate (preferably zinc oxide and/or natural zinc containing materials (preferably ores, minerals, organic salts, polymeric salts or physically adsorbed form material). The zinc-containing layered material is zinc carbonate hydroxide, zinc copper carbonate, layered double hydroxide and/or hydroxy double salts (preferably hydrozincite).

ABEX UPTX: 20031211

ADMINISTRATION - Compositions comprising (I) are administered topically as daily skin or hair care products (e.g. skin lotions, hair sprays and hair gels), as cleansing products (such as shampoos or body washes) or powders (with a carrier such as talc) in an amount of 1-50 g (preferably 1-20 g).

L175 ANSWER 3 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2000-182331 [16] WPIX

DNC C2000-056988

TI Treating schizophrenia and tardive dyskinesia comprises administering tetrahydropyridine compounds as neurotoxic substrates for monoamine oxidase.
DC B03
IN **NELSON, J A**
PA (NELS-I) NELSON J A
CYC 86
PI WO 2000003713 A1 20000127 (200016)* EN 37 A61K031-44
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
AU 9949959 A 20000207 (200029) A61K031-44
US 6232326 B1 20010515 (200129) A61K031-44
ADT WO 2000003713 A1 WO 1999-US15961 19990714; AU 9949959 A AU 1999-49959 19990714; US 6232326 B1 Provisional US 1998-92792P 19980714, CIP of US 1999-232311 19990115, US 1999-353490 19990713
FDT AU 9949959 A Based on WO 2000003713
PRAI US 1999-232311 19990115; US 1998-92792P 19980714; US 1999-353490 19990713
IC ICM A61K031-44
AB WO 200003713 A UPAB: 20000330
NOVELTY - Symptoms of schizophrenia and tardive dyskinesia are treated by administering tetrahydropyridine compounds (I), their pyridinium ions or salts as neurotoxic substrates for monoamine oxidase A and B.
DETAILED DESCRIPTION - Symptoms of schizophrenia and tardive dyskinesia are treated by administering tetrahydropyridine compounds of formula (I), their pyridinium ions or salts as neurotoxic substrates for monoamine oxidase A and B.
R1 = H, methyl, CH2CCH, phenyl or benzyl;
A = phenyl, 5 or 6 membered S or O containing heterocyclyl or 5 or 6-membered cycloalkyl (all optionally substituted);
n = 0 or 1 and
B = C or O.
An INDEPENDENT CLAIM is included for a composition comprising (I) and a selective neural protective agent and/or toxicity-enhancing agent.
ACTIVITY - Neuroprotective; CNS.
MECHANISM OF ACTION - Monoamine oxidase A and monoamine oxidase B inhibitors.
USE - Used for treating schizophrenia and tardive dyskinesia.
ADVANTAGE - The treatment does not cause serious side effects such as symptoms of Parkinson's disease and shows a permanent effect for the long-term. The treatment restores some of the deficient frontal metabolic activity, allowing neurochemical messages sent from the higher cortical structures to the mid-brain to be adequately communicated.
Dwg.0/0
FS CPI
FA AB; GI; DCN
MC CPI: B07-D04A; B07-D04C; B14-D05A; B14-J01B3
TECH UPTX: 20000330
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred compounds: (I) comprises 1-methyl-4-phenyl-1,2,3,6,-tetrahydropyridine (MPTP), 2'-methyl-MPTP, 2'-fluoro-MPTP, 2'-chloro-MPTP, 3'-chloro-MPTP, 3'-bromo-MPTP or 1-methyl-4-tert-butyl-1,2,3,6-tetrahydropyridine and their pyridinium derivatives. The pyridinium ion comprises 2'-methylMPP+, 4'-aminoMPP+, 4'-N(CH3)2-MPP+, 1-methyl-2-phenylpyridinium (sic) or 1-methyl-4-phenylpyridinium.
(I) is administered with a neural protective agent comprising

guanethidine, chloroquine compounds having high affinity to neuromelanin, desipramine, citalopram, 7-nitroindazole (7-NI), estrogen, selegiline (L-(-)-deprenyl), L-(-)-desmethylselegiline, 5-methyl-10,11-dihydro-5H-dibenzo(a,d)cyclohepten-5,10-imine maleate(MK-801)), deprenyl and other monoamine oxidase A (MAO-A) and monoamine oxidase B (MAO-B) inhibitors. The toxicity enhancing agent comprises acetaldehyde (ACE) or **diethyldithiocarbamate** (DDC).

ABEX UPTX: 20000330

ADMINISTRATION - The total dosage is 0.001-0.5 (preferably 0.01-0.2) mg/kg intravenously, orally or intraperitoneally. Three groups of male black mice received injections of MPTP + acetaldehyde at dosages of 5, 10 and 15 mg/kg/day. This regimen was continued for a maximum of 5 days until motor symptoms occurred and did not resolve 24 hours after injections. The data showed a depletion in dopamine level by 50%, 60% and 70% for the respective groups.

L175 ANSWER 4 OF 5 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN
AN **1994-199945** [24] WPIX
DNC **C1994-091317**
TI Compsn. for treatment of ischaemic diseases - comprises calcium channel blocker e.g. verapamil, **diltiazem** etc. and antioxidant.
DC B05
IN HASHIMOTO, M; KUNIHARA, M; LIOU, S
PA (UPJO) UPJOHN CO; (PHAA) PHARMACIA & UPJOHN CO
CYC 47
PI WO 9412185 A1 19940609 (199424)* EN 44 A61K031-55 <--
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CZ DE DK ES FI GB HU JP KP KR KZ LK LU LV MG MN MW NL NO NZ PL PT RO RU SD SE SK UA US UZ VN
JP 06172220 A 19940621 (199429) 30 A61K045-06 <--
AU 9456807 A 19940622 (199436) A61K031-55 <--
EP 682520 A1 19951122 (199551) EN A61K031-55 <--
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 08506096 W 19960702 (199650) 60 A61K045-06 <--
NZ 258768 A 19970424 (199723) A61K031-55 <--
ADT WO 9412185 A1 **WO 1993-US11505 19931202**; JP 06172220 A **JP 1992-324394 19921203**; AU 9456807 A **AU 1994-56807 19931202**; EP 682520 A1 **WO 1993-US11505 19931202, EP 1994-902431 19931202**; JP 08506096 W **WO 1993-US11505 19931202, JP 1994-513408 19931202**; NZ 258768 A **NZ 1993-258768 19931202, WO 1993-US11505 19931202**
FDT AU 9456807 A Based on WO 9412185; EP 682520 A1 Based on WO 9412185; JP 08506096 W Based on WO 9412185; NZ 258768 A Based on WO 9412185
PRAI **JP 1992-324394 19921203**
REP 01Jnl.Ref
IC ICM A61K031-55; A61K045-06
ICS A61K031-135; A61K031-355; A61K031-38; A61K031-40; A61K031-435; A61K031-44; A61K031-445; **A61K031-47**; A61K031-495; A61K031-505; A61K031-56; A61K031-58; A61K047-22
AB WO 9412185 A UPAB: 19971030
Pharmaceutical compsn. comprises a calcium channel blocker and an antioxidant.

The calcium channel blocker is verapamil, **diltiazem**, nifedipine, nicardipine, flunarizine, nilvadipine, nitrendipine, manidipine, benidipine, bepridil or barnidipine and their pharmaceutically active salts especially 2-((4-(2,6-bis(pyrrolidino)-4-pyrimidinyl)-1-piperazinyl)-methyl)-3,4-dihydro-2,5,7,8-tetramethyl-2H-1-benzopyran-6-ol or its pharmaceutically active salts, most pref. 16alpha-methyl-21-(4-(2,6-bis(pyrrolidine)-4-pyrimidinyl)-1-piperazinyl)pregna-1,4,9(11)-triene-3,20-dione or its pharmaceutically

active salts, hydrates or solvates. The antioxidant is a bicyclic amine.
USE/ADVANTAGE - Used in the treatment and prevention of ischaemic diseases (claimed), such as strokes and cerebrovascular diseases that are either post-traumatic or sequela of brain surgery, as well as cardiovascular disorders such as angina pec
and arrhythmic caused upon reflowing of the
damage due to burns, organ transplantation
Dwg.0/0

FS CPI
FA AB; DCN
MC CPI: B01-B03; B06-A01; B06-F03; B07-D03; B0
B14-F02; B14-J01; B14-S08

L175 ANSWER 5 OF 5 WPIX COPYRIGHT 2005 THE THO
AN **1993-054274** [07] WPIX
DNC **C1993-024287**
TI New quinoline and naphthyridine derivs. as
treating hypertension, heart failure, hyper
diabetic retinopathy, migraine, atherosclerosis, cognitive disorders etc..
DC B02
IN CHAKRAVARTY, P K; GREENLEE, W J
PA (MERI) MERCK & CO INC
CYC 10

PI	EP 527534	A1 19930217 (199307)* EN	45	C07D215-22	<--
	R: CH DE FR GB IT LI NL				
	CA 2075652	A 19930214 (199318)		C07D215-233	<--
	US 5246944	A 19930921 (199339)	24	C07D215-20	<--
	JP 06056789	A 19940301 (199413)	30	C07D215-22	<--

ADT EP 527534 A1 **EP 1992-202422 19920805**; CA 2075652 A **CA 1992-2075652 19920810**; US 5246944 A **US 1991-744140 19910813** ; JP 06056789 A **JP 1992-215991 19920813**
PRAI **US 1991-744140 19910813**
REP 1.Jnl.Ref; EP 323841; EP 412848; EP 470794; EP 487252; EP 490587; WO 9107404; WO 9111999; WO 9112001; WO 9202508
IC ICM **C07D215-20**; **C07D215-22**; **C07D215-233**
ICS A61K031-435; **A61K031-47**; A61K031-535; A61K031-675; C07D401-12; C07D403-12; C07D405-12; C07D413-12; C07D471-04; C07D491-056; C07F009-547
AB EP 527534 A UPAB: 19940126
Substd. benzyloxy- quinoline and 1,5-naphthyridine derivs. of formula (I) and their salts are new.
In (I) R1 = H, 1-8C alkyl, 3-8C cycloalkyl, 3-8C cycloalkyl (1-4C alkyl), 1-8C perfluoroalkyl, Ph or Ph (1-4C alkyl); R2 = H, 1-8C alkyl, 3-8C cycloalkyl, 3-8C cycloalkyl (1-4C alkyl), CO2R5a, 1-4C alkoxycarbonyl, CN, NO2, Ph or Ph (1-4C alkyl); R3, R4 = H, 1-6C alkyl opt.substd. by 1 of Ph, naphthyl, 3-7C cycloalkyl, NR5R21, morpholin-4-yl, OH, CO2R5a or CON(R5)2), 1-6C alkoxy, 1-4C perfluoroalkoxy, halo, CF3, CN, NO2, OH, NH2, NH (1-6C alkyl), N(1-6C alkyl)2, N(CH2CH2)2O, N(CH2CH2)2NCOR5a, N(CH2CH2)2NR5a, CO2R5a, CONH2, 1-4C alkoxycarbonyl, CONH(1-7C alkyl) or CON(1-7C alkyl)2; or R3 + R4 = 1-4C alkylenedioxy; x = 0-2; m = 1-5; n = 1-10; E = CH or N; R5 = H or 1-6C alkyl; R5a = R5, CH2Ph, CH2-naphthyl, Ph or naphthyl; R9, R10 = H, 1-6C alkyl (opt. substd. by 3-7C cycloalkyl), 2-6C alkenyl, 2-6C alkynyl, halo, 1-6C alkoxy, 1-6C perfluoroalkyl, 3-7C cycloalkyl, Ph, naphthyl, 1-6C alkyl-S(O)x-(Ch2)n, HO(1-6C alkyl) CF3, CO2R5a, Oh, NR5R21, 1-6C alkyl-NR5R21, NO2, (CH2)n-SO2-N(R5)2, NR5CO(1-4C alkyl) or CON(R5)2; or R9 + R10, when on adjacent C atoms, = Ph; X = O, S(O)x, NR13, CH2O, CH2S(O)x, CH2NR13, OCH2, NR13CH2, S(O)xCH2, CH2, (CH2)2 or a bond; or X = -CH=, in which case Y and R12 are absent; Y = a bond, O, S(O)x, NR13 or CH2; provided that the C to which Z is attached is not bonded to 2 heteroatoms; R11, R12 = H, 1-6C

alkyl (opt. substd. by 1 of Ph, naphthyl, NR5R21, 3-7C cycloalkyl, morpholin-4-yl, OH, CO2R5a or CON(R5)2), Ph, naphthyl, Ph (1-2C alkyl) or naphthyl (1-2C alkyl) (all opt. substd. by 1-3 from halo, 1-6C alkyl, 1-5C alkenyl-CH2, 1-5C alkynyl-CH2, 1-6C alkyl-S(O)n(CH2)n, CF3, CO2R5a, OH, NR5R21, NO2, NR5COR5, CON(R5)2, G(1-6C alkyl)R23, N(CH2CH2)2Q3 and P(O)(O(1-4C alkyl))2, and additionally opt. substd. by 1-2 from Br, Cl and F) or 3-7C cycloalkyl. New compsn. comprises (I), a carrier and opt. another anti-hypertensive agent (diuretic, ACE inhibitor, Ca channel blocker or beta-blocker) (amiloride, atenolol, bendroflumethiazide, chlorothalidone, chlorothiazide, clonidine, cryptenamine acetates and tannates, deserpidine, diazoxide, guanethidene sulphate, hydralazine HCl, hydrochlorothiazide, metolazone, metoprolol tartrate, methyclothiazide, methyldopa, methyldopate.HCl, minoxidil, pargyline HCl, polythiazide, prazosin, propranolol, rauwolfia serpentina, rescinnamine, reserpine, sodium nitroprusside, spironolactone, timolol maleate, trichlormethiazide, trimethophan camsylate, benzthiazide, quinethazone, ticrynafen, triamterine, acetazolamide, aminophylline, cyclothiazide, ethacrynic acid, furosemide, merethoxylline procaine, sodium ethacrynate, captopril, delapril.HCl, enalapril, enalaprilat, fosinopril Na, lisinopril, pentopril, quinapril HCl, ramipril, teprotide zofenopril Ca, diflusinal, **diltiazem**, felodipine, nicardipine, nifedipine, niludipine, nimodipine, nisoldipine, nitrendipine, etc, and admixtures and combinations of these.

USE - (I) are angiotensin II antagonists and are useful for treating hypertension, acute and chromic congestive heart failure, secondary hyper aldosteronism, prim. and sec. pulmonary hyperaldosteronism, prim. and sec. pulmonary hypertension, renal failure e.g. diabetic nephropathy, glomerulonephritis, sclerodema, glomerular sclerosis, proteinuria of prim. renal disease, end stage renal disease renal transplant therapy etc, renal vascular hypertension, left ventricular dysfunction, diabetic retinopathy and vascular disorders e.g. migraine, Raynaud's disease, luminal hyperplasia, and to minimise atherosclerosis. (I) are also useful for treating ocular hypertension. In addition, (I) have CNS activity and are useful in the treatment of cognitive dysfunction (e.g. Alzheimer's disease, amnesia and senile dementia) and to relieve anxiety and tension in patients with depressed or dysphoric mental states. (I) also have antidopaminergic activity and are useful to treat disorders involving dopamine dysfunction (e.g. **schizophrenia**). Admin. is oral, rectal, parenteral or (for ocular treatment), topical, at a daily dose of 1-1000 mg, pref. 2.5-250 mg, especially 2.5-75 mg (cardiovascular and ocular disorders) or 5-6000 mg, pref. 10-4000 mg, especially 20-2000 mg (CNS disorders), opt. in divided doses.

Dwg.0/0

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B05-B01E; B06-D02; B06-D06; B12-A07; B12-C06; B12-C10; B12-D01; B12-F01B; B12-F05A; B12-G03; B12-G04A; B12-H03; B12-H05; B12-K06; B12-L04

ABEQ US 5246944 A UPAB: 19931123

Substd. quinolines and azaquinolines (1,5-naphthyridines) oxymethylene bridged to substd. phenyl derivs. of formula (I) and salts are new. In the formula, R1 is H, 1-8C alkyl or -perfluoroalkyl, R2 is H, 1-8C alkyl, 5-8 cycloalkyl and -cycloalkylalkyl, CO2R5a, CN, NO2, Ph or Phalkyl, R3 and R4 are H, 1-6C alkyl opt. substd. 1-6C alkoxy, 1-4C perfluoroalkyl, CF3 or 1-4C alkoxycarbonyl, x is 0-2, E is CH, R5 is H or 1-6C alkyl, R5a is R5, CH2aryl, where aryl is Ph or naphthyl or aryl is as in R5b, R9 and R10 are H, 1-6C alkyl opt. substd. 1-6C alkenyl or -alkynyl or -alkoxy or -perfluoroalkyl, 3-7C cycloalkyl, opt. substd. 1-6CalkylS(O)xC(CH)n or OHalkyl, X is O, (S)Ox, NR13, CH2 etc. Y is bond, O, S(O)xNR13, CH2, R11

and R12 are H, 1-6C alkyl, opt. substd. aryl or 3-7C cycloalkyl, R13 is H, 1-6C alkyl, aryl, 1-6CCalkylCO, 2-5C alkenylCH2, Z is CO2H, CO2R24, tetrazol-5-yl, CONH(tetrazol-5-yl), and R14 is 1-4C alkyl, x is 0-2.

USE - (I) are angiotensin II antagonists used to treat hypertension, esp. ocular hypertension and also cognitive dysfunction, anxiety and depression.

Dwg.0/0

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=> d his

     (FILE 'HOME' ENTERED AT 07:41:00 ON 21 DEC 2005)
               DEL HIS

     FILE 'HCAPLUS' ENTERED AT 07:42:16 ON 21 DEC 2005
L1             2 S US20040229908/PN OR US2003-616692#/AP,PRN
               E NELSON J/AU
L2          1574 S E3-E52
               E NELSON JODI/AU
L3            16 S E3-E5
               E ALPHA/PA,CS
               E ALPHA RES/PA,CS
L4             1 S E13-E16
L5             3 S L1,L4

     FILE 'REGISTRY' ENTERED AT 07:45:14 ON 21 DEC 2005
               E CHLOROQUINE PHOSPHATE/CN
L6             1 S E3
L7            24 S 54-05-7/CRN AND P/ELS
L8            20 S L7 AND 7664-38-2/CRN
L9             4 S L7 NOT L8
               E CIMETIDINE/CN
L10            1 S E3
L11           69 S 51481-61-9/CRN
L12            0 S L11 AND L8
L13            6 S L8 NOT MXS/CI
L15           11 S L*** NOT (COMPD OR CONJUGATE OR WITH)
L16           30 S L*** NOT L15
L17            6 S L6,L13
L18           12 S L10,L15

     FILE 'HCAPLUS' ENTERED AT 07:49:45 ON 21 DEC 2005
L19          771 S L17
L20          667 S (CHLOROQUIN# OR CHLORCHIN#)()(PHOSPHATE OR DIPHOSPHATE OR DIH
L21          234 S AVLOCLOR OR ARECHIN OR ARALEN()(PHOSPHATE OR DIPHOSPHATE) OR
L22           14 S SN 7618 OR NSC 14050 OR WR 1522 OR SN7618 OR NSC14050 OR NSC
L23         1069 S L19-L22
L24         5067 S L18
L25         8050 S CIMETIDIN# OR ACIBILIN OR ACINIL OR BIOMET OR CIMAL OR CIMETA
L26            0 S SKF92334 OR SKF 92334 OR SKF 92 334 OR NSC335308 OR NSC 33530
L27         8253 S L24-L26
L28            9 S L23 AND L27
L29            3 S L28 AND L1-L5
L30            7 S L28 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L31            4 S L30 NOT L29
               SEL HIT RN L29

     FILE 'REGISTRY' ENTERED AT 07:56:34 ON 21 DEC 2005
L32            2 S E1-E2
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L33           2 S L32 AND L17,L18

     FILE 'REGISTRY' ENTERED AT 07:56:53 ON 21 DEC 2005

     FILE 'HCAPLUS' ENTERED AT 07:57:00 ON 21 DEC 2005

     FILE 'REGISTRY' ENTERED AT 07:57:25 ON 21 DEC 2005
               E 591.79/RID
               E 591.79.52/RID
L34       363017 S E3
L35            6 S (CELECOXIB OR CHLORPHENIRAMINE OR FLUOXETINE OR PAROXETINE OR
L36            9 S (AMIODARONE OR CLOMIPRAMINE OR LEVOMEPROMAZINE OR METOCLOPRAM
L37            9 S (INDINAVIR OR NELFINAVIR OR SAQUINAVIR OR AMIODARONE OR CIPRO
L38            6 S (FLUVOXAMINE OR ITRACONAZOLE OR KETOCONAZOLE OR MIFEPRISTONE
               E DELAVIRIDINE/CN
L39            1 S E1
               E NORFLOXACINEM/CN
L40            1 S E2
               E DIETHYL DITHIOCARBAMATE/CN
               E DITHIOCARBAMATE/CN
               E C5H11NS2/MF
L41           69 S E3
L42            4 S L41 AND DIETHYL
L43            2 S L42 NOT (13C OR LABELED)
L44           33 S L35-L40,L43

     FILE 'HCAPLUS' ENTERED AT 08:07:30 ON 21 DEC 2005
L45               TRA L29 1- RN :      233 TERMS

     FILE 'REGISTRY' ENTERED AT 08:07:31 ON 21 DEC 2005
L46          233 SEA L45
L47           32 S L46 AND L44
L48            1 S L44 NOT L47
               SEL RN L47
L49         1862 S E1-E32/CRN
L50         1189 S L49 NOT (MXS OR PMS OR IDS)/CI
L51          364 S L50 NOT (COMPD OR WITH OR LABELED OR CONJUGATE)
L52          354 S L51 NOT H
L53           10 S L51 NOT L52

     FILE 'HCAPLUS' ENTERED AT 08:09:16 ON 21 DEC 2005
L54        10279 S L52
L55        61759 S L47
L56        14065 S CELECOXIB OR CHLORPHENIRAMIN# OR  FLUOXETINE OR PAROXETINE OR
L57        19948 S AMIODARONE OR CLOMIPRAMINE OR LEVOMEPROMAZINE OR METOCLOPRAMI
L58        42458 S INDINAVIR OR NELFINAVIR OR SAQUINAVIR OR AMIODARONE OR CIPROF
L59         8909 S FLUVOXAMINE OR ITRACONAZOLE OR KETOCONAZOLE OR MIFEPRISTONE O
L60         1019 S DELAVIRDINE OR NORFLOXACINEM OR DIETHYL DITHIOCARBAMATE
L61        10445 S DIETHYLDITHIOCARBAMIC ACID OR DIETHYLDITHIOCARBAMATE
L62       101369 S L27,L54-L61

     FILE 'REGISTRY' ENTERED AT 08:12:46 ON 21 DEC 2005
L63          142 S L34 AND L46 NOT L47,L52
L64          141 S L63 NOT L17

     FILE 'HCAPLUS' ENTERED AT 08:14:00 ON 21 DEC 2005
L65         5629 S L64
L66         6449 S L23,L65

     FILE 'REGISTRY' ENTERED AT 08:14:19 ON 21 DEC 2005
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L67       362658 S L34 NOT L6,L7,L44,L47,L49
L68       312879 S L67 AND 1/NC
L69       306617 S L68 NOT (PMS OR CCS OR IDS OR MNS)/CI
L70       306104 S L69 NOT SQL/FA
L71       105066 S L70 AND ED<=1999
L72       201038 S L70 NOT L71
L73         9075 S L72 AND ED<=2000

     FILE 'HCAPLUS' ENTERED AT 08:17:27 ON 21 DEC 2005
L74        83387 S L71
L75         1650 S L73
L76        13929 S (A61K031-47 OR C07D215)/IPC
L77        93905 S L66,L74-L76
L78         4834 S L77 AND L62
L79         3464 S L78 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L80            4 S L78 AND L1-L5

     FILE 'REGISTRY' ENTERED AT 08:26:26 ON 21 DEC 2005
L81            2 S 329322-82-9 OR 330597-62-1

     FILE 'HCAPLUS' ENTERED AT 08:26:31 ON 21 DEC 2005
L82           45 S L81 AND L77
L83            3 S L82 AND L1-L5
L84            4 S L80,L83
L85            7 S L82 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L86         3463 S L79,L85 NOT L84
                 E NERVOUS SYSTEM/CT
L87       333287 S E3+OLD,NT
L88            8 S E2
L89       103409 S E3-E96
L90        33636 S E99-E204
L91         9577 S E96,E97,E205-E216
L92       224670 S E240+OLD,NT
L93        13731 S E240-E300
L94         3347 S E301-E318
L95         1367 S E319-E329
                 E NEURON/CT
L96        19335 S E3
L97            1 S E57
                 E SCHIZOPHRENIA/CT
L98        10378 S E3-E7 OR E3+OLD,NT
                 E PARKINSON/CT
L99        15152 S E7-E9 OR E7+OLD,NT
                 E E7+ALL
                 E E13+ALL
L100        4895 S E4
                 E E12+ALL
                 E E14+ALL
L101        1219 S E5+NT
                 E E4+ALL
L102       22498 S E4+NT
                 E NERVE/CT
L103      167288 S E3+OLD,NT
L104      145870 S E3-E48
L105       34989 S E49-E96
L106       51767 S E97-E132
L107       30329 S E133-E180
L108       17918 S E181-E212
L109       11853 S E218-E228 OR E220+OLD,NT
L110       11092 S E229-E282
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L111      52327 S E314 OR E317-E336 OR E319+OLD,NT
L112      14304 S E337-E372
L113      22876 S E373-E395
L114      13911 S E396
L115       1524 S E397-E401
                E MOTOR/CT
L116        215 S E27
                E COGNITI/CT
L117       9282 S E4+OLD,NT OR E4-E8 OR E11+OLD,NT OR E12
                E E13+ALL
L118        996 S E2,E3
                E MENTAL/CT
L119      14032 S E22,E23
L120      24566 S E29-E90
                E E29+ALL
L121      58762 S E8+OLD,NT
                E BRAIN/CT
                E E3+ALL
L122     397625 S E4+OLD,NT
L123        218 S L86 AND L87-L122
L124          1 S L123 AND ?DYSKINES?
L125         12 S L123 AND ?PARKINSON?
L126          3 S L123 AND ?SCHIZOPHREN?
                E METABOLISM/CT
                E E13+ALL
L127         45 S E2,E3(L)PERIPHER?
L128        217 S E2+NT(L)PERIPHER?
L129          0 S L123 AND L127,L128
L130          2 S E2+OLD,NT AND L123
L131          4 S L84 AND L87-L122
L132          2 S L84 AND E2,E3
L133          4 S L131,L132
L134         15 S L124-L126
L135          1 S L134 AND L30
L136         14 S L134 NOT L135
                SEL DN AN 7 9
L137          2 S L136 AND E1-E6

     FILE 'WPIX' ENTERED AT 08:56:16 ON 21 DEC 2005
L138      12745 S (A61K031-47 OR C07D215)/IPC
L139      27371 S D621/M0,M1,M2,M3,M4,M5,M6
L140         35 S L20/BIX OR L21/BIX OR L22/BIX
                E CHLOROQUINE/CN
L141          5 S E3-E11
                SEL SDCN
                EDIT /SDCN /DCN
L142        225 S E1-E6
                E QUINOLINE/CN
L143          1 S E3
                SEL SDCN
                EDIT /SDCN /DCN
L144        338 S E1
L145        661 S 0579/DRN
L146      35931 S L138-L145
L147       8218 S L25/BIX OR L26/BIX OR L56/BIX OR L57/BIX OR L58/BIX OR L59/BI
                E CIMETIDINE/CN
L148          4 S E3-E8
                SEL SDCN
                EDIT /SDCN /DCN
L149        468 S E1-E6
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L150       8340 S L147-L149
L151       1127 S L146 AND L150
L152          3 S L151 AND NELSON J?/AU
L153         76 S (A61P021 OR A61P025)/IPC AND L151
L154        142 S L151 AND P617/M0,M1,M2,M3,M4,M5,M6
L155         21 S L153 AND L154
L156         63 S L154 AND (P446 OR P510 OR P517)/M0,M1,M2,M3,M4,M5,M6
L157          6 S L154 AND (B14-J01A3 OR C14-J01A3 OR B12-C04 OR C12-C04)/MC
L158         13 S L154 AND (B14-J01B3 OR C14-J01B3 OR B12-C10 OR C12-C10 OR B12
L159          9 S L154 AND (B14-J05 OR C14-J05)/MC
L160         65 S L155-L159
L161          9 S L151 AND ?DYSKINES?
L162         63 S L151 AND ?PARKINSON?
L163         33 S L151 AND ?SCHIZOPHREN?
L164          9 S L151 AND (?METABOL?(L)?PERIPHER?)
L165          2 S L164 AND L161-L163
L166          2 S L164 AND L160
L167          1 S L166,L165 NOT BRAZZALE?/AU
L168          3 S L152,L167
L169        127 S L160-L164 NOT L165-L168
L170         15 S L169 AND PY<=1999
L171         32 S L169 AND PRY<=1999
L172         29 S L169 AND AY<=1999
L173         32 S L170-L172
               E R00107+ALL/DCN
               E R11285+ALL/DCN
               SEL DN AN 22 24 L173
L174          2 S L173 AND E1-E4
L175          5 S L168,L174

     FILE 'WPIX' ENTERED AT 09:27:11 ON 21 DEC 2005

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